

SURGICAL PATHOLOGY

BY

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110 ILLUSTRATIONS



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TO
MY WIFE
MARGARET
AND DAUGHTERS
LINDA AND PAULA
FOR CHEERFULLY PERMITTING
MANY HOURS OF NEGLECT

With the development of the many specialties in the field of medicine and with the advent of the certifying boards, the surgical pathologist is constantly approached by the prospective examinee for recommendation of a source from which to study pathology in his respective field. This book is designed to serve as this source—to cover adequately the major surgical specialties, namely, ear, nose and throat, general surgery, urology and gynecology. While none of the subdivisions is exhaustively treated, each is considered with enough detail to give the specialist a basic understanding of his particular subject.

The book is also designed to aid the surgical pathologist and the surgeon who often wish only to refresh their memories as to the salient points rather than to wade through a mass of sometimes irrelevant detail. For all concerned two ideas have been kept in mind: (1) to treat the subject from a regional viewpoint, and (2) to summarize, as far as possible, the current ideas from the current literature.

With regards to the text itself, the material must of necessity be incomplete. For example, in the chapter on the skin it would be impossible to cover all the lesions without writing a separate book. For this reason only those cutaneous conditions which are more commonly encountered in a general hospital such as ours have been described. The brain and spinal cord have been omitted, for this is regarded as an entirely different field—a specialty in itself. A brief account of the embryology, anatomy and histology of each system has been included because these subjects are deemed extremely important for a thorough understanding of pathology, and if they are not before the reader in concise form, he is too often reluctant to look them up. To accomplish this the following textbooks were freely consulted:

Arey, Leslie Brainerd. *Developmental Anatomy. A Textbook and Manual of Embryology*. Fourth Edition. W. B. Saunders Co., Philadelphia, 1943.

Lewis, W. H. *Gray's Anatomy*, Twenty-fourth Edition. Lea & Febiger, Philadelphia, 1942.

Maximow, Alexander A., and Bloom, William. *A Textbook of Histology*. Fourth Edition. W. B. Saunders Co., Philadelphia, 1944.

Finally, enough clinical material is included to bridge the gap between what are often called the preclinical and the clinical sciences in an attempt to make pathology a living subject.

My thanks are due many people. Both the attending and resident staffs have been most helpful and coöperative in securing material suitable for photographing. I particularly wish to thank Dr. C. J. Bucher for valuable aid, Dr. P. C. Swenson for the roentgenograms, Mr. Allen F. Hancock for the photography, Mr. J. J. Wilson, our librarian for his assistance, and Dorothy Ewald Bauer for the secretarial work.

PETER A. HERBUT

PHILADELPHIA, PA

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Surgical Pathology

Chapter I

SKIN AND SUBCUTANEOUS TISSUE

EMBRYOLOGY AND HISTOLOGY

THE skin is composed of an outer portion—the epidermis, which arises from the ectoderm, and an inner portion—the corium, which arises from the immediately subjacent mesoderm. In the first few weeks of embryonic life, the epidermis consists of a single sheet of

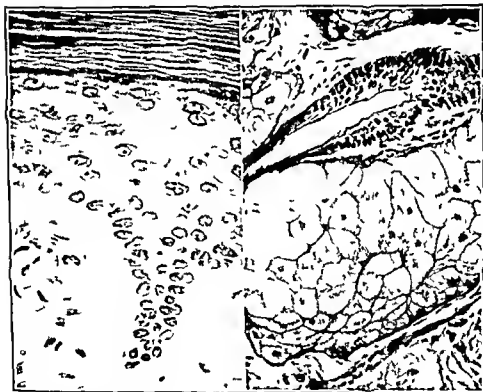


FIG 1

FIG 2

FIG 1—Normal skin showing from above down stratum corneum stratum granulosum stratum germinativum composed of polyhedral prickle cells with distinct intercellular bridges and a basal cell layer a rete cone in the center and papillae on either side of the latter $\times 400$

FIG 2—Normal hair hair follicle and sebaceous gland The characteristic cell of the latter is large polygonal with distinct reticulated cytoplasm and small round nucleus $\times 200$

cuboidal cells Gradually, differentiation occurs so that at birth

regeneration of the hair follicle. Attached also to the hair is the arrector pili which arises from the surrounding mesenchyme. *Sebaceous glands* are scattered all over the body except in the palms and soles. Most arise from, and empty into, the hair shafts but some originate directly from the surface epidermis. They are bounded externally by a basement membrane of connective tissue along which is lined a single layer of flat cells containing round nuclei. These give rise to the innermost mass of large polyhedral cells. Initially, the latter resemble the prickly cells of the epidermis but as they grow older they gradually become distended with fat droplets. Ultimately, the entire cell is destroyed and the fatty material is liberated as secretion (holocrine gland). Most *sweat glands* arise directly from the surface epidermis although some also arise from the hair shafts. They consist of a duct and a secretory portion. In the epidermis the former is lined with concentric epidermal cells while in the dermis it is lined with a double layer of thin epithelial cells. The secretory portion consists of coiled glands which are composed of an outer basement membrane, an intermediate layer of flat spindle cells (myoepithelium) and an inner single layer of cuboidal cells (Fig 3). The surface of these cells often contains small pieces of pinched off cytoplasm which allegedly forms part of the secretion and the glands are, therefore, called apocrine glands.

PATHOLOGY

Congenital Anomalies—More frequently than not, most congenital abnormalities of the skin are of greater cosmetic importance to the patient than they are of real danger. Almost all of the normal constituents of the integument arising from ectoderm are known to participate in anomalous developments, and because of the frequency with which multiple structures are involved in the same patient the lesions are often grouped under the title of "*congenital ectodermal dysplasia*." Thus the epidermis may give rise to *ichthyosis*—an excess thickening of the stratum corneum, or portions of it may be pinched off to produce midline *epithelial inclusions*. Alterations in the amount of pigment give rise to *albinism*—when it fails to form or *melanism*—when it forms in excessive amounts. Abnormal formation of pigment producing cells gives rise to *nevi* or *moles*. The appendages too participate in anomalous developments. The nails may fail to form—*anonychia*, the hair may be overabundant—*hypertrichosis* or *hirsutism*, less than the normal amount—*hypotrichosis*, or completely absent—*atrachosis*, the *sebaceous glands* may be hypoplastic, absent or blocked, and the *sweat glands* may be underdeveloped or entirely absent. Congenital lesions of mesodermal origin are less numerous and only two need be mentioned here—*osteoma* and *angioma*. Of all the afore-mentioned anomalies only three—midline epithelial inclusions, nevi and angioma—are frequent enough to warrant further comment.

Midline Epithelial Inclusions—The midline of the body both anteriorly and posteriorly represents the line of fusion of two lateral

composed of many layers of flat, keratinized, dead cells, (2) stratum lueidum composed of several layers of flat, closely packed, clear cells without nuelei, (3) a narrow stratum granulosum consisting of three to five layers of flat cells in the eytoplasm of which are found small granules and (4) stratum germinativum composed of several layers of large, polyhedral, priekle cells covering a single layer of euboidal or cylindrical basal cells. All these layers, however, are identifiable only in the skin of the palms and soles whereas elsewhere the coreum, priekle cells and basal cells alone are discernable. In all areas the inner surface of the epidermis is thrown into pyramidal projections, called rete cones which point into the dermis. Pigment granules are added to the basal layer shortly after birth.

The *corium* is composed of collagen and elastic fibers and is dividable into a compact superficial portion and a loose, fatty, deep portion. It contains numerous blood and lymph vessels, nerves and nerve endings, seattered pigmented cells and epidermal appendages. The latter consist of nails, hairs, sebaceous glands and sweat glands.

The *nails* first appear at ten weeks as a thickening of the epidermis and then grow proximally to the level of the first phalanx. They regenerate from the proximal portion—the nail root—and in the adult form consist of closely welded, eornified, epithelial cells. The *hairs* develop at three months as downgrowths of the germinal cells

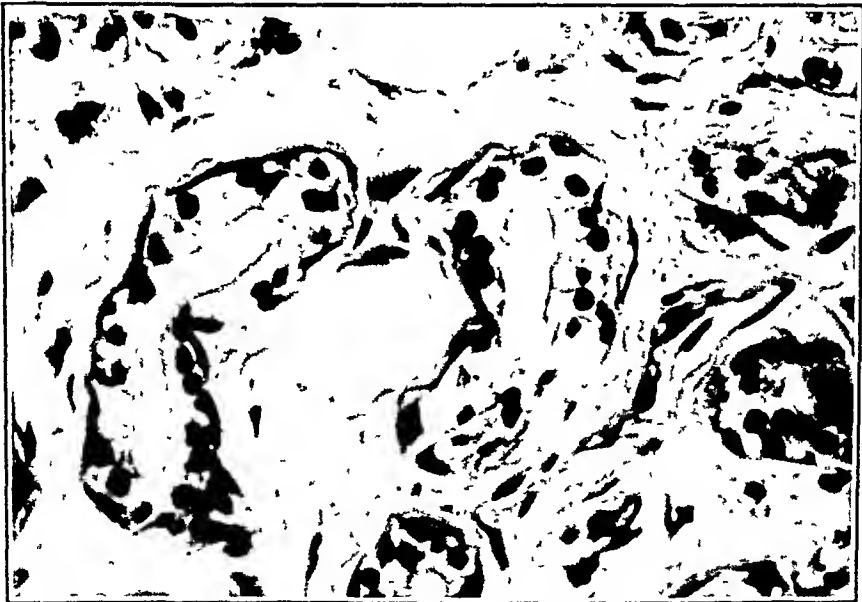


FIG. 3 ~ Normal sweat gland showing from without in a basement membrane, a single layer of flat myoepithelial cells and a single row of cuboidal cells $\times 100$.

of the epidermis (Fig. 2). The initial buds consist of outer columnar cells continuous with the basal cells of the epidermis, an inner mass of polyhedral cells, and a bulbous base that covers a nugget of connective tissue which forms the papilla. The basal cells covering the latter actually give rise to the hair substance. Protruding from the under surface of the hair are two swellings— an upper which forms the sebaceous gland and a lower which contributes to the

stratified squamous epithelium is present in about two thirds of the cases whereas in the rest this has been replaced with granulation tissue (Fig 4). The wall may contain sebaceous and sweat glands



FIG 4—Pilonidal sinus showing a lining of stratified squamous epithelium, a diffuse infiltration with plasma cells and lymphocytes and two giant cells of the foreign body type $\times 200$

The surrounding inflammation is non-specific and consists of plasma cells, lymphocytes, monocyte phagocytes, neutrophils and sometimes giant cells of the foreign body type

The diagnosis is made from a history of recurrent pain and discharge and upon the demonstration, in the sacrococcygeal region, of a dimple, sinus, cyst or abscess

Treatment consists of complete surgical excision of the tracts and the surrounding inflammatory tissue. Failure to do so accounts for recurrences which occur in about 25 per cent of cases. The ultimate prognosis is excellent.

Nevus—The term nevus is often used to designate a birth mark and as such covers both the common mole and the angioma. Its use here however, is restricted to the former. They are common congenital lesions of the skin that are either present at birth or appear at any time thereafter. Nevi are located anywhere on the body

but are commonly found about the face, neck and trunk. They are solitary or multiple, vary in size from less than a millimeter to many centimeters, and are hairy or non-hairy, warty or flat, and non-pigmented or grey, brown, black or blue (Fig 5)



FIG 5—Pigmented hairy nevus

plates of ectoderm. In the process of development it is common for the fusion to be incomplete resulting in the formation of epithelial lined fistulas or sinuses, or for pieces of ectoderm to be trapped at the points of closure, lie dormant for varying intervals and then as a result of stimulation, to grow and form epithelial lined cysts. Such anomalies have been described at the root of the nose, in the lower lip, floor of the mouth, sternum urachal region, perineal raphe and over the sacrum and coccyx. The latter, known as pilonidal sinus, is the most common and will be considered in more detail. Urachal anomalies are fully described in the section on the urinary bladder.

Pilonidal Sinus.—This is a sinus or a cyst communicating with, or lying beneath, the epidermis that covers the lower portion of the sacrum and the coccyx. It has been described under many *other names*, some of which are sacral, coccygeal or sacrococcygeal infundibulum; dermoid and dermoid fistula, sinus or cyst; posterior umbilicus; postanal dermoid; congenital dermal sinus, and sacrococcygeal ectodermal sinus. That the lesion is congenital there is no doubt but its genesis is still not settled. From a study of human embryos there is evidence to suggest a twofold *origin* (1) that it is a remnant of the medullary canal and (2) that it results from a faulty fusion of the ectodermal covering in early embryonic life. There is, however, no support for two other theories that have been advanced (1) that it is analogous to the preen gland in birds and (2) that it is a remnant of a vestigial secondary sex gland. Its incidence is about 1 in 940 hospital admissions. It is found in three males to every female and the average age is about twenty-one years. Why the lesion remains symptomless until this time of life is not entirely understood. The growth stimulus has been attributed to direct trauma, increased physical activity in general, and to hormonal influences. Evidence for the latter lies in the fact that hormones do regulate body growth, and particularly skin and hair, and it is just beyond the age of puberty that the disturbance first becomes manifest. *Symptoms* consist of pain in the sacrococcygeal region, often associated with a watery or creamy discharge. Examination discloses a dimpling, or one or more sinuses in the midline of the skin covering the sacrum and coccyx. Rarely, the opening may be a few centimeters to one side of the midline and in a few cases, it has been reported at a higher level. In these the condition is more serious for the sinus then communicates with the spinal canal. When the process is active, the surrounding skin and subcutaneous tissue show the usual signs of inflammation or frank abscess. In 10 per cent of cases, there is no communication with the surface and the lesion is that of a frank cyst.

Grossly, the pathological specimen is usually covered on the epidermal side with methylene blue—a dye injected to determine the extent of the lesion. Usually the main sinus communicates with many branching sinuses in the dermis and subcutaneous tissue or it may lead to a cyst or frank abscess. Hair is present in the lumen of the sinus or cyst in about half the cases. The wall and surrounding tissue is thick and fibrous. *Histologically*, a lining of

They have been considered to arise from (1) the covering epithelium (2) mesoderm and (3) the terminal nerves. Because of the frequently close apposition of neural cells to the overlying skin, it was for many years believed that cells from the epidermis migrated into the subjacent corium to produce the tumor. This theory has slowly lost its appeal and today its few remaining advocates are to be found only among dermatologists. Proponents of the mesodermal theory point to the striking similarity between blue nevi and *Mongolian spots*. The latter are flat, often ill-defined, dull blue areas of pigmentation found in the skin over the sacrum and occasionally elsewhere. They were first described in Mongolian infants but are now known to occur in infants of all races. Histologically, they are composed of oblong or spindle cells with centrally placed, evenly stained, round nuclei and a moderate amount of cytoplasm. On the polar side of the nucleus the cytoplasm contains accumulations of brown pigment. These cells are located in the deeper portions of the corium and are true melanoblasts. Their location and appearance, however, does not preclude a mesodermal origin, for it is in exactly the same location that Masson and Foot have described similar cells and have demonstrated their origin from the nerve sheath—the sheath of Schwann. The epithelioid-like cells found in the more superficial portions of nevi, these authors have likened to Meissner's corpuscles or Merkel-Ranvier cells. Thus the origin of nevi from nerve tissue seems to be clearly established. Ludlaw and Murray have not only confirmed these studies but have suggested that the pigmented mole in man represents the tactile spots of reptiles and amphibians!



FIG 7—Large elevated capillary hemangioma (strawberry birthmark) (Courtesy of Dr. T. P. Fierhard)

The diagnosis is made from the gross appearances of the lesions which have been already enumerated. Sometimes they are confused with a pigmented papilloma or a sclerosing hemangioma. It is the consensus that treatment is unnecessary unless the nevus is in a location where it is constantly irritated or unless it begins to grow. In either case it should be surgically excised and it should be excised both widely and deeply enough, for incomplete removal may result in a cancerous transformation. Irradiation is without effect. When one considers the fact that almost everybody harbors a mole or two, and that there are comparatively few melanoblastomas, it is apparent that the prognosis, generally speaking, is excellent. One must, however, at the same time remember that occasionally an excised nevus is by all present histologic standards benign and yet it may give rise to widespread metastasis either immediately or many years after removal.

Ordinarily they remain quiescent throughout life, but occasionally, as a result of trauma, continued irritation or spontaneously, they may become malignant (melanoblastoma) and are then deadly. This is particularly true of the blue—black, non-hairy, flat type of nevus.

Histologically, nevi are composed of neval cells which in reality are melanoblasts. These vary somewhat according to whether they are located in the superficial or in the deeper portions of the corium. The former are rather large pale polyhedral and epithelioid-like (Fig. 6). Their cytoplasm is pale and distinct and

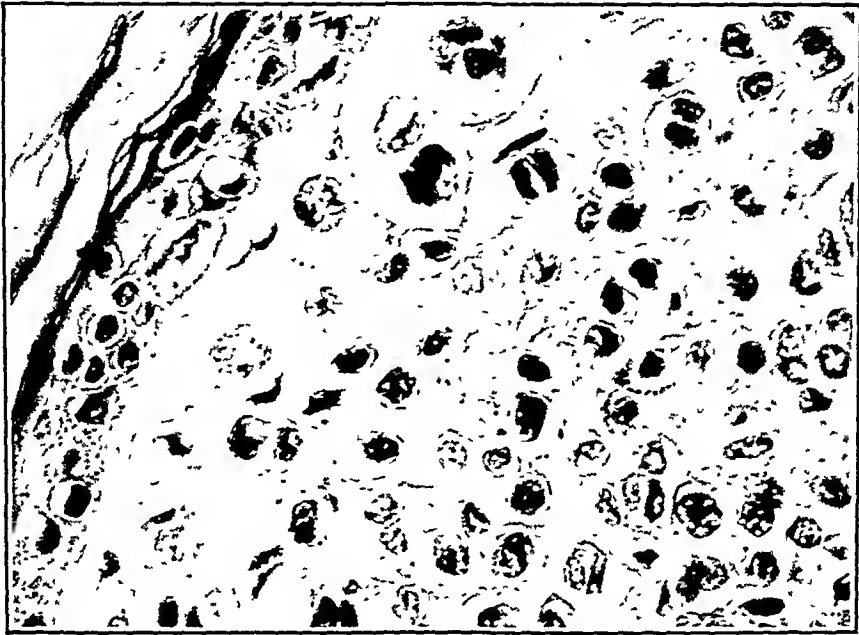


FIG 6 —Pigmented nevus showing large pale polyhedral neval cells some of which contain melanin. x 400.

their nuclei are round, oval and evenly stained. In the deeper layers they tend to become elongated, more fusiform and may be seen closely connected with nerve fibers. The cells are arranged in clusters, groups, strands or large sheets and while they are not encapsulated they are relatively well demarcated from the surrounding corium. In ordinary histologic sections, melanin pigment may be entirely absent or it may be so abundant as to obscure the underlying cells. It is present in the neval cells themselves, in the basal cells of the covering epidermis, and in irregular wandering phagocytic cells (chromatophores). The latter are branching, fusiform or spindle shaped cells that are often found around the periphery of the tumor. In the non-pigmented variety pigment can be demonstrated in abundance in older neval cells by the *dopa* (3,4-dioxyphenylalanin) reaction. This reaction is apparently dependent upon the presence of an oxidase within the cytoplasm of melanoblasts which reacts with *dopa* to produce a brown pigment that is closely allied to melanin.

The *histogenesis* of pigmented nevi has been a subject for considerable debate and is one which is still not completely settled.

This type almost always disappears spontaneously within a few months or several years and, therefore, requires no treatment (2)

Capillary These are well-defined, bright red, slightly elevated, superficially situated tumors that measure as much as several centimeters in diameter and 2 cm in thickness and that blanch poorly on pressure (Figs 7 and 8) Histologically, they are composed of capillary blood vessels exhibiting a well-differentiated endothelium (Fig 9) The stroma is either scanty and composed

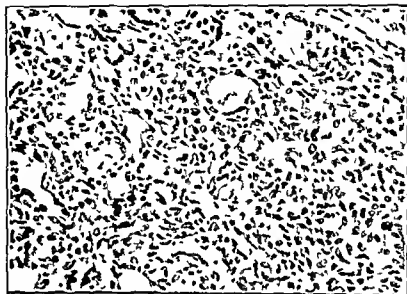


FIG 9—Capillary hemangioma showing numerous endothelial lined, thin walled capillaries and a cellular stroma $\times 200$

of delicate connective tissue or abundant and composed of oblong endothelial cells similar to those lining the capillaries In the latter it may be so abundant as to almost completely obscure the vessels themselves (3) *Cavernous* These are soft, elevated, poorly circumscribed, dark or purplish blue, easily compressible and blanchible tumors that extend deeper into the subcutaneous tissue and may grow to considerable proportions (Fig 10) They are composed of dilated thin-walled spaces lined with endothelium and filled with blood (Fig 11) Sometimes they are mixed with the capillary type Because of a concomitant excessive supply of blood these tumors may be associated with a hypertrophy of the surrounding tissue and adjacent bones (4) *Port wine stain* These are flat irregular deep red to purple patches that are found most often on the face and neck They are composed of a very narrow zone of dilated vessels lined with flat, adult endothelium and are located just beneath the epidermis (5) *Cirsoid* This is a rare type of hemangioma that appears rather suddenly in adults and is located almost entirely about the face and neck It is a soft, bulky, bluish-red pulsating tumor that has a tendency to establish communications with larger vessels as for example the carotid artery In some cases, because of arterial pulsations, it destroys local tissue and

Angioma.—An angioma is a tumor composed of blood vessels and called a *hemangioma*, or of lymph vessels and called a *lymphangioma*. Each is congenital in origin and each arises from sprouts or buds of endothelial cells which later become canalized.

Hemangioma.—This lesion is exceeded in frequency only by the pigmented nevus. In three quarters of the cases it is evident at birth, and in the rest it is probably present at birth but is not discovered until later. Two thirds of the cases are encountered in males and one third in females. This distribution is so constant



FIG 8 —More diffuse, only slightly elevated capillary hemangioma

that a hormonal *cause* for the tumor has been postulated. In support of this theory it has been pointed out that the onset of menses or the beginning of pregnancy sometimes ushers in a rapid increase in size of the lesions. Hemangiomas are single in 85 per cent of cases and multiple in 15 per cent. One half of the lesions are found on the head and neck, one quarter on the trunk and one quarter on the extremities. They can be conveniently divided into *six* different types. (1) *Hemangioma simplex* (naevus simplex, telangiectasia nuchae of the newborn). This consists of blotchy, ill-defined, pale red, not elevated, easily blanched areas situated in the skin of the nape of the neck in 33 per cent of all newborn infants.

morrhuate. Of all these methods irradiation is the most popular not only because it is easy to administer but because if properly applied it leaves the least scarring. It is, however, not without danger and if injudiciously used it may result in scarring, telangiectasia, residual tumor, increased pigmentation, atrophy of the skin, alopecia, ulceration and epiphyseal injury. The prognosis in hemangiomas as far as health is concerned is excellent but cosmetically it sometimes leaves much to be desired. On rare occasions histologically entirely benign hemangiomas have been known to produce widespread metastases.



FIG. 11.—Cavernous hemangioma illustrating large spaces lined with flat endothelium and filled with erythrocytes. $\times 200$

Lymphangioma—A lymphangioma is a definite tumor not merely a group of dilated lymphatic channels. Its incidence as compared with hemangioma is about 1 in 25. Over one half of the lesions are noted at birth, almost all are discovered before the age of ten years and the sites of predilection are the head, neck and extremities. Lymphangiomas can be divided into three types: (1) *Simple lymphangiomas*. These are uncommon simple dilations of the subepithelial lymphatic channels that externally appear as small circumscribed wart-like elevations. (2) *Cavernous lymphangiomas*. These constitute most of the tumors of the lymphatic channels. They are found in the skin and subcutaneous tissue anywhere over the body but may also be found in the mouth or deep between muscle bundles. They range in size from a few millimeters to that involving an entire extremity. The more superficial lesions are manifest as multiple brown or red, vesicopapules or even papillary excrescences, whereas the deeper ones are manifest as multiple diffuse spongy compressible nodules or masses usually covered by normal skin. Histologically they are composed of dilated lymphatic vessels lined by a single or multiple layer of flat endothelial

also result in a fatal hemorrhage. Histologically, it consists of thick-walled, tortuous arterioles and proliferating capillaries. (6) *Sclerosing hemangioma*: This category includes all hemangiomas that show a tendency to regression either as a result of injury, surface ulceration or infection, or more important, perhaps, spontaneously. The lesions are limited to the skin and subcutaneous tissue in all parts of the body; they vary in size from a few millimeters to several centimeters; they are flat, smooth, pink, grey, yellow, tan or brown, and in one half of the cases they are found after the age of thirty years. Fundamentally the process consists of an overgrowth of the connective tissue stroma which may be cellular and fibroblastic or acellular and collagenous. The amount may be slight or it may be severe enough to entirely obliterate the original lesion. The blood vessels thus are choked off; their endothelial

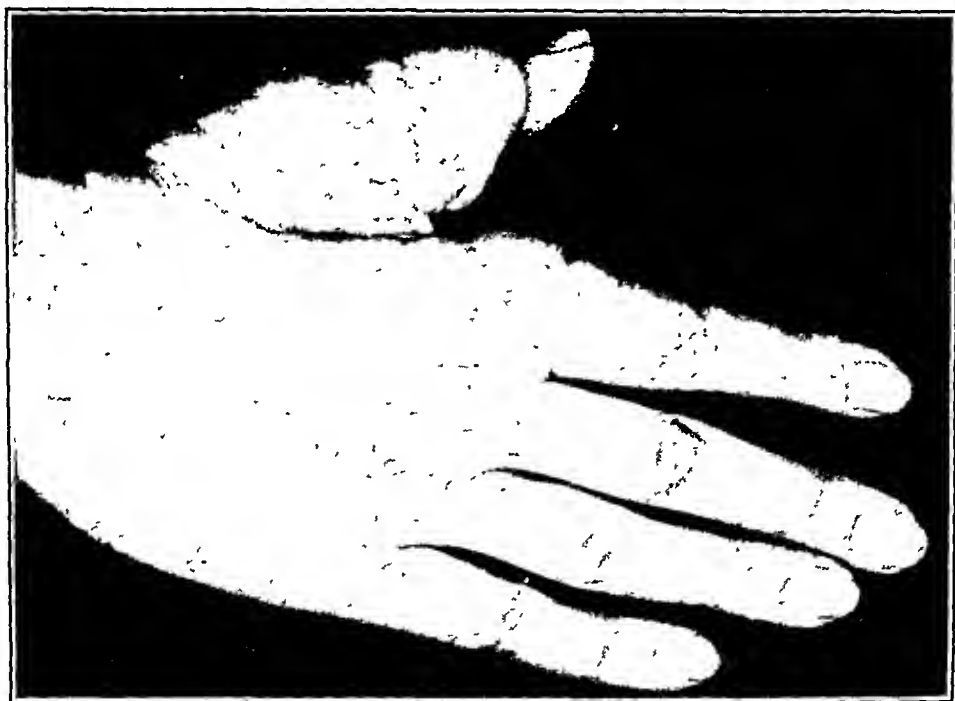


FIG. 10 —Large boggy cavernous hemangioma of the right thumb and index finger.

cells coalesce to form giant cells of the foreign body type; there is an accumulation of large foam cells, and scattered throughout there are varying amounts of hemosiderin pigment. Little wonder then that the lesion is, both grossly and histologically, often mistaken for a fibroma, xanthoma or a pigmented nevus!

Ordinarily, there is no difficulty in making a *diagnosis* of hemangioma from the gross appearance of the lesion. *Treatment* varies according to the size and type of lesion and its location. Some, particularly those in the nape of the neck, will disappear spontaneously while others, such as the port wine stain, if treated at all must be excised surgically. The methods of treatment in use today may be listed as irradiation (radium, radon, roentgen ray), surgery, electrosurgery, carbon dioxide snow, and injection with sodium

almost become synonymous with a suppurative inflammation of the loose subcutaneous connective tissue. A *phlegmon* has much the same connotation except that the process is further advanced, leads to suppuration and ulceration, and is often accompanied by constitutional disturbances. An *abscess* is a localized area of suppuration contained within a pocket and eventuates from a disintegration of the tissue itself. A *paronychia* is a purulent inflammation of the skin and subcutaneous tissue lateral to a fingernail. Three acute inflammatory lesions of the skin that deserve more than passing comment are furuncle, carbuncle and human bite.

Furuncle—A furuncle or boil is an acute abscess of the dermis that starts in a hair follicle, and less commonly in a sebaceous or sweat gland. The causative *organism* in most instances is *staphylococcus aureus*. What brings about the infection is not entirely clear, although it is generally conceded that lowering of skin resistance is an important factor. This is accomplished by (1) a low peripheral blood supply brought about by a low basal metabolic rate and subnormal temperature, (2) general debilitating conditions as uncontrolled diabetes mellitus, leukemia, anemia and avitaminosis and (3) local factors such as humid, dusty atmosphere, perspiration, and irritation of clothing. Persistence of the afore-mentioned conditions is likewise responsible for the recurring crops of boils which is so characteristic of this disease. *Grossly*, a furuncle appears as a raised, red, tender, hot, tense painful swelling that measures a few millimeters to several centimeters in diameter. Its central portion soon undergoes necrosis and liquefaction and it heals by discharging its contents onto the surface. A few, however, do not reach maturity but regress and disappear spontaneously. Since a furuncle is never excised or even incised in its initial stages, one rarely has the opportunity to study the early inflammatory changes. By the time an odd specimen reaches the pathologist, it consists of an ordinary *acute pyogenic abscess*. It is composed of a central area of bacteria and nuclear fragments surrounded by neutrophils and, at the periphery, varying numbers of lymphocytes, plasma cells, fibroblasts, capillaries and even foreign body giant cells. Because of recurring attacks the morbidity in furunculosis is high but the mortality rate is low. The seriousness of boils lies not in the lesion as such, but in the *complications* which sometimes develop. These consist of a progression to form carbuncles, of septicemia with metastatic abscesses, and of acute ulcerative endocarditis. *Treatment* consists of removing the underlying cause if this can be determined, of administering penicillin intramuscularly, of irradiation therapy and of evacuating the pus surgically.

Carbuncle—A carbuncle is a group of furuncles originating in adjacent hair follicles, sebaceous glands or sweat glands. In about one half of the cases, particularly in men, they are located on the back of the neck, and in the other half they are found in diminishing order of frequency on the face, trunk, arms, legs, and scalp. Males are affected three times as frequently as females and in each the majority of patients are over thirty years of age. The local signs and symptoms are similar to, but more profound than, those in

cells. Their lumens are empty or are filled with lymph and rarely with blood. The stroma of connective tissue varies in amount and may contain lymphoid and muscle tissue or, in the more aggressive tumors, it may consist entirely of proliferating endothelial cells. (3) *Cystic hygroma*: These are cystic tumors of lymphatic channels that originate in the same primordia as do normal lymph vessels. As such they are usually found in the neck, retroperitoneum and along the iliac vessels or in the groin. They are generally present at birth, grow rather rapidly and consist of compressible, multiple thin-walled cysts filled with serous fluid (Fig. 12). Histologically



FIG. 12 —Cystic hygroma There are numerous large and small cystic spaces imparting a sponge-like appearance to the tumor.

the cysts are lined with flattened endothelial cells and are supported by a stroma of fibrous tissue.

Of value in the *diagnosis* of lymphangioma is the history of the tumor since birth, the vesicopapules or warty nature of the superficial lesions and the boggy, spongy compressible consistency of the deeper tumors which characteristically lack the discoloration of hemangiomas. Despite scarring and a tendency to postoperative keloid formation, *surgical excision* followed by roentgen irradiation offers the best *prognosis*. In cystic hygromas postoperative infection is very common and the *mortality rate* is as high as 47 per cent.

Inflammation.—**Acute Inflammation.**—Acute inflammation of the skin and subcutaneous tissues is very common. In most cases the organisms gain entrance by direct implantation from the surface. Usually they produce mild infections that attract little attention and require little or no treatment but at other times the lesions are more serious and may be fraught with graver consequences. The latter fall into the following well-defined categories. *Cellulitis*—literally an inflammation of cells but through usage the term has

Syphilis—Syphilis is a chronic infectious disease caused by *treponema pallidum*. This is a slender thread-like, tightly coiled, motile organism with pointed ends. It is about 8 to 12 microns in length and 0.5 microns in diameter. It stains with difficulty but can be demonstrated by Giemsa's stain, Wright's stain and silver impregnation. The simplest and best method of identifying the organism in early syphilis is by dark field illumination. In later stages of the disease it is difficult or impossible to demonstrate the organism by any method. The cutaneous manifestations of acquired syphilis may be conveniently divided into three stages.

Primary Stage or Chancre—The chancre occurs in from twelve to forty days after contact at the point of inoculation and is, therefore, found most frequently on the genital organs. Extragenital chancres on the lip, tongue, tonsil, finger, nipple and elsewhere on the skin, while not common, do occasionally occur. The lesion is usually single but may be multiple. It varies in size from 1 mm. to 10 cm. or more, although ordinarily it is not larger than 1 cm. in diameter. It is raised, flat, sharply defined, extremely firm, painless, indurated at the base and superficially eroded or ulcerated (Fig. 13). Its



FIG. 13—Chancre of the penis. The lesion is raised, firm, sharply defined and superficially ulcerated.

floor is clean and is either of a beefy red color or covered with a thin grey membrane from which oozes a serous exudate. The chancre disappears in from three to eight weeks often leaving a thin, atrophic scar. In about three quarters of the cases there is a concomitant non-suppurative enlargement of the draining lymph nodes. The histologic changes in the chancre are quite characteristic. There are present edema and a diffuse, dense infiltration with lymphocytes and plasma cells. Capillaries are quite numerous and the inflammatory cells are characteristically stuffed about these and about

furunculosis. In addition, however, there are often general disturbances consisting of malaise, fever, and leukocytosis. The predisposing and immediate causes of a carbuncle are the same as those of a furuncle. Forty per cent of cases have had previous furuncles or carbuncles and an equal number give a history of various other infections. Because the edges of the lesion gradually fade into the surrounding tissue the exact size is difficult to determine but some measure as much as 15 cm. across. The more superficial inflammations disclose a taut, red, warm surface in which there develop, at an early stage, numerous small sinuses that discharge pus onto the surface. When the infection is more deeply situated the entire area is extremely firm, indurated, fixed to the surrounding structures and ulcerates much later. Cut surfaces disclose numerous abscesses of varying sizes separated by bands of dense fibrous tissue. The *histologic* appearance is that of an acute abscess and indistinguishable from a furuncle. Although over fifty different methods of *treatment* have been recorded, some sort of surgical interference, irradiation, and application of compresses are universally employed. Alongside of these penicillin will undoubtedly take its place. The *death rate* is about five per cent and approximately half of these are in patients with diabetes. The systemic complications are the same as those in furuncles.

Human Bite.—This is a common lesion, for the literature contains reports of some 700 cases and doubtlessly there are many others that have not been recorded. The infection is found most frequently in young, white, male adults in the third decade of life. Most of the injuries are sustained by actually biting, a lesser number in fights by hitting one's opponent in the mouth, and only a few result from gnawing at fingernails and sucking fingers. Although the *lesions* are found anywhere on the body the fingers and hands are most frequently involved, and because of nearness of sheaths, tendons, joint spaces and bones these constitute the most serious infections. In neglected or mistreated cases a dusky redness and swelling appear about the wound in from four to twenty-four hours and this is soon followed by a thin, grey, foul discharge. Pain is usually severe and there may be chills, fever, headache, malaise and leukocytosis. Depending upon the extent of injury the infection may remain localized to the lacerated area or it may *spread* to the underlying and adjacent structures. Accordingly there may be soft tissue necrosis, abscess, suppurative tenosynovitis, osteomyelitis, arthritis, lymphangitis and lymphadenitis. The *organisms* responsible for the necrotizing process are the fusiform bacillus, Vincent's spirochaetes and bacterium melanogenicum. Two principles should be followed in treating human bites (1) convert the wound from an anaerobic to an aerobic state and (2) excise all devitalized tissue that may contain bacteria. The mortality rate is 1 per cent.

Chronic Inflammation.—In a book of this scope it would be impossible to attempt even a summary of the diversified chronic infections of the skin. Only a few of the more commonly encountered lesions, therefore, will be described.

Papular lesions are a progression of macular syphilides. They vary in size from 1 mm. to 2 cm. or more, are raised, rounded or flat, and are either smooth on the surface or are covered with a scale. When the latter is removed they exhibit a coppery color. Histologically they are similar to macules except that the cellular infiltration is much more severe. *Follicular syphilides* occur at the mouths of hair follicles as small rounded papules. The inflammatory reaction, however, is less severe than it is in the true papule. Follicular lesions have a tendency to group together and to contain an excess amount of pigment. On the scalp they are accompanied by a loss of hair—alopecia. *Pustular syphilides* are uncommon. They consist principally of indolent ulcers with a conical heaping up of crusted material.

Tertiary Stage—Following the secondary eruptions there may be a short period where no lesions are manifest or there may be several "recurrences" of irregular types of lesions that are different from those in the second stage and not typical of those in the late stage. At any rate tertiary lesions appear at any time from two to thirty years after inoculation. Unlike their predecessors these cutaneous infections occur in fewer numbers or are solitary. They are usually asymmetrical, deeply infiltrative, indolent, sharply delineated, nodular and smooth or ulcerated. They have a tendency to central or one-sided healing with peripheral extension of the lesion and hyperpigmentation about their margins. In addition to these there is the solitary gumma which arises as a cutaneous or subcutaneous tumor of a pink and later a darker red or blue color. Sooner or later most gummas undergo general softening, perforate onto the surface and discharge viscous pus, or they slough in a mass leaving a granulating ulcer. Occasionally, however, a gumma may resolve without breaking down.

Histologically tertiary lesions are of two types—*diffuse inflammatory and gummatous*. The former is by far the more frequent. It consists of a diffuse infiltration of the entire area with lymphocytes and plasma cells that have a distinct tendency to be grouped about the vessels, and of a varied degree of fibroblastic proliferation. In addition there are two vascular lesions that are very characteristic. One is frequently recognized and consists of a proliferating, obliterative endarteritis, while the other is less frequently noted and consists of a periendophlebitis. The latter is in reality nothing more than a gradual infiltration of the walls of the veins from without in by syphilitic granulation tissue. Ultimately the lumen is filled with granulations, the muscle and connective tissue of the wall are entirely destroyed, and all that remains are the split up remnants of elastic fibers. In early stages the venous lesion can be recognized in ordinary hematoxylin and eosin stained preparations but in late stages the obliterated and destroyed vein can be recognized only by stains that demonstrate elastic tissue fibers. The *gumma*, histologically, is quite characteristic (Fig 15). It consists of a central mass of necrosis which, however, is not quite as complete as that in tuberculosis for ghosts of former structures can often be readily discerned and outlines of vessels can be easily detected with elastic

arterioles (Fig. 14). The latter respond with a marked proliferation of the endothelial cells which in turn reduces the vascular lumen, decreases the blood supply and results in superficial necrosis and sloughing of the epidermis. At the margin of the ulcer the epithelium frequently undergoes marked proliferation so that it may be mistaken for an early squamous cell carcinoma. With the onset of healing the edema subsides, the inflammatory cells disappear, fibrosis supervenes and the epithelium regenerates completely or sometimes incompletely leaving a thin, fine, grey scar.

Secondary Stage.—Ordinarily the secondary stage of syphilis becomes manifest, in from six to ten weeks after inoculation, in the

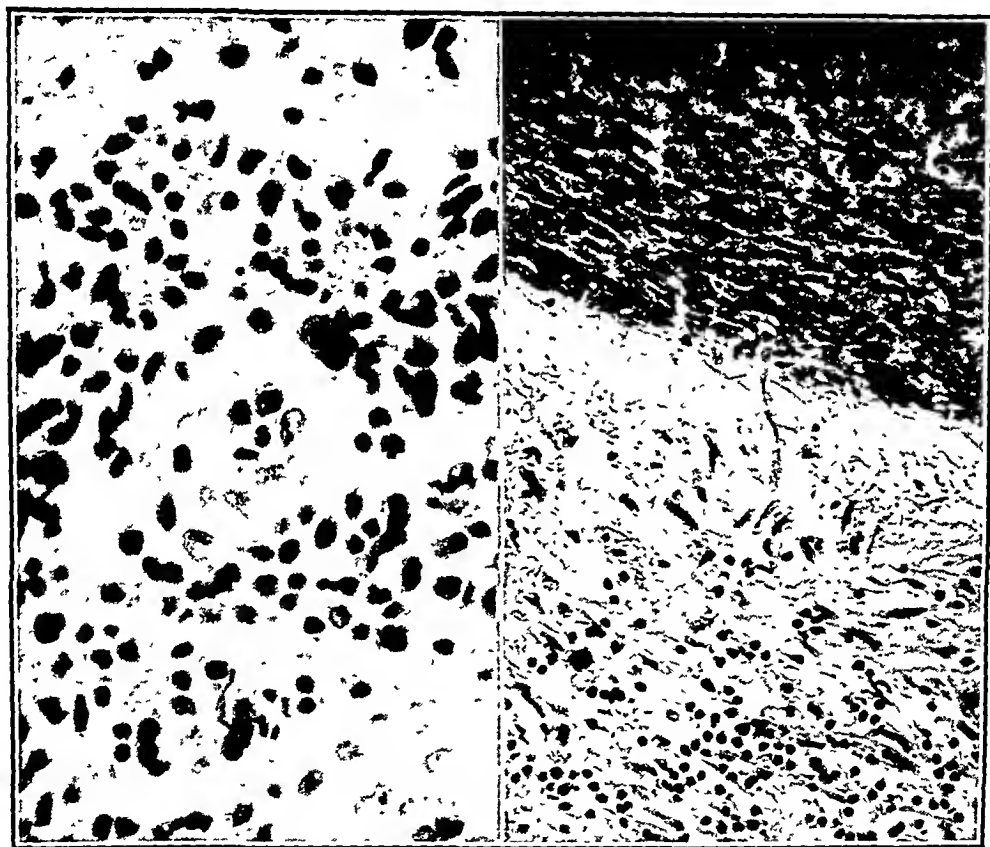


FIG. 14

FIG. 15

FIG. 14.—Chancre showing proliferative endarteritis and a perivascular infiltration with plasma cells and lymphocytes. $\times 400$.

FIG. 15.—Gumma illustrating a sharply defined mass of necrosis. Peripherally there are fibroblasts, capillaries, plasma cells and lymphocytes $\times 200$

form of eruptions on the skin and mucous membranes. These vary tremendously in appearance so that they may be mistaken for a host of other lesions. Unlike other infections, however, they have a symmetrical distribution and tend to be arranged in a semicircle. Despite individual variations secondary lesions of the skin can be grouped into four categories, namely, macular, papular, follicular and pustular. *Macular* syphilides consist of faint pink spots from a few millimeters to a centimeter or more in diameter. They are due to dilated engorged capillaries supported by a somewhat edematous stroma that contains only a few plasma cells and lymphocytes.

spread at the periphery. The surrounding skin frequently discloses a variable amount of brown pigment.

Histologically, the characteristic unit is the tubercle, although in the skin it is not always as typical as it is in some of the other organs and tissues. Its structure depends a great deal upon whether it is the first or subsequent infection of the host, the number and virulence of the organisms, the liquefying power of the neutrophils and the patency and abundance of blood vessels. Early in its development the tubercle is composed of a non-specific infiltration of neutrophils and a few lymphocytes. In its typical and completely developed form it consists of a central collection of epithelioid cells in which there is often a small focus of caseation necrosis and is surrounded by a few giant cells of the Langhans' type (Fig 16). About the periphery there are a ring of lymphocytes,

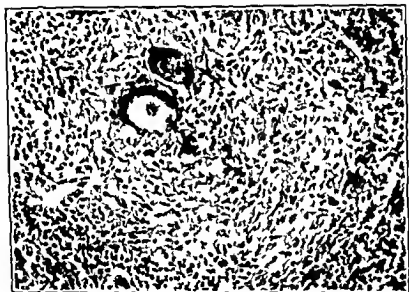


FIG 16—Tubercle composed of epithelioid cells with early central necrosis, eccentric giant cells of the Langhans' type and a surrounding lymphocytic and plasma cell infiltration. $\times 200$

variable numbers of plasma cells and, beyond these, a fibroblastic reaction. Epithelioid cells are derived from the reticulo-endothelial system. They are fairly large cells with an abundant amount of rather ill-defined cytoplasm and round or oblong centrally placed, evenly stained, light blue nuclei. Langhans' giant cells arise from epithelioid cells either as a coalescence of several nuclei or as a result of division of the nuclei and failure of a corresponding division of the cytoplasm. They consist of a large mass of cytoplasm with a partial or complete ring of peripheral nuclei. In cutaneous tuberculosis virtually any single component of the tubercle can predominate over the others, or be entirely absent, thus resulting in a variety of histologic appearances. The tubercles may be discrete or confluent, they may be found in any portion of the dermis but are often grouped about hair follicles or sweat glands, they have a

tissue stains. About the periphery there are many lymphocytes, few plasma cells, scattered epithelioid cells, fibroblasts and capillaries. Occasionally a few giant cells of the Langhans' or foreign body type are also present, but ordinarily they are in complete abeyance. Miliary gummas about the periphery of the larger ones are not to be found and this in itself helps to distinguish a gumma from a tubercle.

The cutaneous manifestations of *congenital syphilis* are essentially the same as those in the secondary and tertiary stages of acquired syphilis. The chancre is not seen.

A *diagnosis* of syphilis is made from a history of contact, gross examination of the characteristic lesions, dark field demonstration of *treponema pallida* from primary and secondary sores, and a positive blood Wassermann. Histologic confirmation is of particular value in tertiary lesions but is not a routine procedure in primary or secondary eruptions. In the past *treatment* of syphilis consisted of the administration of arsphenamine, bismuth, mercury and iodides. Currently, excellent results are being reported in both early and late syphilis following the use of intensive penicillin therapy, and it appears as though this drug might replace the others. The *prognosis* in syphilis depends upon the extent and type of visceral involvement.

Tuberculosis.—Tuberculosis of the skin is a fairly common disease that affects people of all ages and both sexes. It is, of course, caused by the *tubercle bacillus* and is contracted either by direct local inoculation through the epidermis or by hematogenous or lymphatic metastasis from other foci in the body. The cutaneous lesion enlarges by extension to contiguous tissues and also by secondarily invading the blood and lymphatic channels. The infections may involve any part of the body but are found most frequently about the face, head, neck and upper extremities. On the basis of gross and microscopic appearances dermatologists have subdivided tuberculosis of the skin into over fifteen different varieties and to each have attached cumbersome names. Since variations are often slight and since there is considerable overlapping of the different lesions it seems that such subdivisions are not only unnecessary but that they are both confusing and superfluous. Hence in this chapter names will for the most part be omitted and a concise description of the variable cutaneous sores will alone be submitted.

Tuberculous *lesions* of the skin vary in size from a fraction of a millimeter to over 8 cm. in diameter. They may be superficial, intracutaneous or subcutaneous. Sometimes the smaller lesions are distinctly grouped around hair follicles but more often a predilection for specific cutaneous structures cannot be discerned. The sores appear as nothing more than mere oval areas of discoloration, as flat or elevated indurations, or as distinct sharply circumscribed nodules with a doughy feel. The colors are variable and consist of combinations of brown, red, blue, purple, grey and yellow. The covering epidermis may be intact and smooth, scaly, horny, vesicular or pustular, or it may be ulcerated. The edges of the latter are characteristically irregular, sharp, soft and undermined. Ulcerated lesions often have a tendency to heal in the center and simultaneously

body but are most frequent on the face and upper extremities. The characteristic histologic unit in Boeck's sarcoid is the hard tubercle. This is composed of a solid nest of large, pale staining, epithelioid cells that occasionally show some destruction in the center but never any caseation necrosis (Fig 17). About the periphery there may be a few lymphocytes and plasma cells, although these are not numerous enough to form mantles as they do in tuberculosis. Giant cells of the Langhans' type are sparse or entirely absent. Occasionally, they contain irregular, bluish stained, calcific inclusions that are said to be characteristic for the disease. Generally speaking,

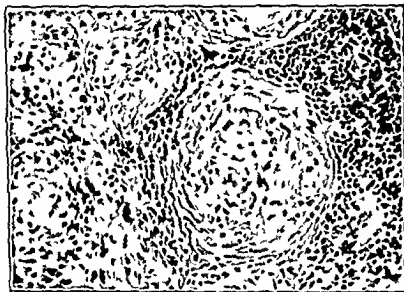


Fig. 17.—Boeck's sarcoid showing small solid sharply circumscribed collections of epithelioid cells. $\times 200$

the miliary tubercles do not coalesce and the lesions enlarge by the formation of new foci. In the skin the infiltrations are initially found in the outer part of the dermis and as they enlarge they infiltrate the deeper portion, in lymph nodes and other organs they have an irregular distribution, and in bones they are found in the medullary cavity.

The cause of sarcoidosis is not known. Because, however, histologic transitions between Boeck's sarcoid and ordinary tuberculosis have been recorded, and because most of the deaths in sarcoidosis are due to tuberculosis, many authors believe that sarcoidosis is a form of tuberculosis, or at least that the two diseases are very closely related. The diagnosis is easily made clinically when the lesions are present in the skin, lymph nodes and bones but it should always be confirmed histologically. Roentgenologically, the osseous changes consist of punched out areas of decreased density or of a diffuse rarefaction of the medulla of particularly the phalanges of the fingers and toes. Treatment is symptomatic. The course is protracted. Some of the lesions regress spontaneously and completely, and heal by fibrosis, but others progress and after many years those patients often die of tuberculosis.

tendency to spread along blood and particularly lymphatic vessels; they destroy all the underlying structures including elastic tissue, and, as a result of vascular occlusion or direct pressure, they produce ulceration of the overlying epidermis. Along the edges of the defect the latter responds in a proliferative manner sending down finger-like projections of epithelium which may be mistaken for cancer and occasionally, in cases of long standing, actually produce a carcinoma of the epidermoid type. Simple proliferative changes of the epithelium are prone to occur in the chronic sinuses seen in *scrofuloderma* (caseating tuberculosis of lymph nodes and bones that secondarily involve the skin). Both proliferation and *carcinoma* (2 per cent of cases) are seen in *lupus vulgaris* (superficially ulcerating tuberculosis commonly seen on the face).

A *diagnosis* of tuberculosis of the skin is made from the gross appearance of the lesions, which, however, are not always characteristic, from histologic sections of tissue secured at biopsy, and above all by isolating the tubercle bacilli. These can be readily found in properly stained histologic sections in early lesions and somewhat less frequently in caseating foci, but they are demonstrable with great difficulty in tubercles showing little or no caseation. In such cases the organism can often be recovered in cultures and in guinea pigs inoculated with tuberculous tissue. *Treatment* is directed towards building up body resistance. The course is protracted. The *prognosis* is good in the localized form but is poor in the disseminated hematogenous variety.

Boeck's Sarcoid.—Boeck's sarcoid is a chronic specific granulomatous disease that is disseminated throughout the body but characteristically involves the skin, lymph nodes and bones. It affects the colored race three times as frequently as the white, is found most often between the ages of twenty to thirty-five years, and has no predilection for either sex. The disease has been known for half a century and has been described under several *other names* some of which are, multiple benign sarcoid, miliary benign lupoid, lupus perino, benign lymphogranulomatosis, non-caseating tuberculosis, Besnier-Boeck's disease, and Besnier-Boeck-Schaumann disease. The term sarcoid was used by Boeck for he thought the lesion resembled sarcoma and it is retained here only because of popular usage.

The lesions in the skin are of *three types*. (1) *Discrete nodular*: These consist of small sharply circumscribed, firm intracutaneous nodules that measure as much as 5 mm. in diameter. Young lesions are bright red and smooth but older ones are dark brown and are covered with fine scales. (2) *Large nodular*: The early lesions in this group are similar to those in the first group but as they enlarge they form nodules that measure as much as 3 cm. in diameter. At this stage the center is blue and retracted, and about the periphery there are light brown spots. The nodule is firm and shows no evidence of breaking down or ulceration. The surface is covered with fine scale. (3) *Diffuse infiltration*: These lesions are ill-defined, firm, intracutaneous indurations of variable size and of a blue or bluish red discoloration. They are found anywhere on the

(Fig 18) In addition to those forming clumps, the causative organisms are diffusely scattered throughout connective tissue cells, vascular endothelium and phagocytic cells

The *maculoanesthetic* lesions start either as irregular, circular, red spots that enlarge peripherally or less often as vesicles. Simultaneous involvement of the nerve endings produces first hyperesthesia and later anesthesia and, as the lesions progress, nodules develop along the course of the peripheral nerves. *Histologically*, the changes in the dermis are non-specific and are similar to the early lesions that precede the nodular formations already discussed



Fig 19—Blastomycosis. Intraepithelial abscess showing numerous doubly refractile budding spores, leukocytes and degenerating cells. $\times 400$

The essential lesion in the nerves is a massive proliferation of the perineurium and endoneurium with a destruction of the nerve fibers themselves

Mycoses—Mycotic infections of the skin are not too common but are extremely important both because they resist treatment and because they mimic so many other diseases. Five different types of infection will be briefly considered here—blastomycosis, actinomycosis, sporotrichosis, coccidioidomycosis and histoplasmosis.

Blastomycosis of the skin may arise as a result of direct inoculation from without, as an extension from a deeper lesion or as a metastasis from a distant focus. Consequently the infection may involve the superficial or the deep portions of the skin. The former appears as papules that enlarge, soften, ulcerate, discharge their contents onto the surface, crust, heal by scarring and give rise to new lesions by direct implantation. The deeper lesions are larger masses that become fluctuant and in time likewise rupture onto the surface. *Histologically*, the changes in the epidermis are very characteristic. There are slight hyperkeratosis, marked proliferation and downward extension of the rete cones, and intraepithelial abscesses. The

Leprosy is a chronic infectious disease caused by mycobacterium leprae and characterized by the formation of specific granulomata. It is never found in infants, is sometimes seen in children and usually becomes manifest after the age of twenty years. Males are somewhat more frequently affected than females. The causative *organism* is a gram positive, acid fast, often beaded and curved rod that appears very similar to the tubercle bacillus. It is found with ease in histologic sections from fully developed lesions but it has never been satisfactorily cultivated on artificial media. Animal inoculation of leprous material has likewise not resulted in the

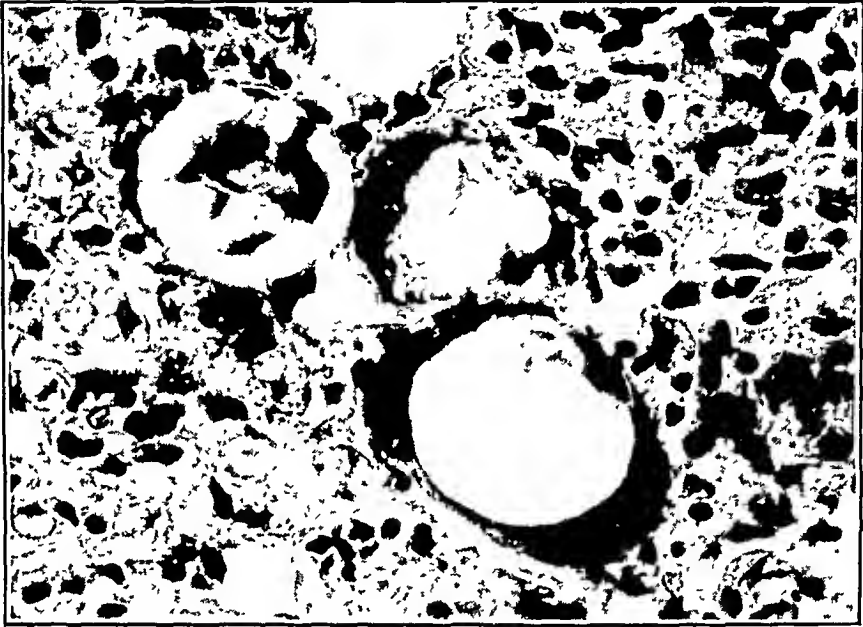


FIG. 18 —Leprosy illustrating three leprosy cells which contain globi. Two of the cells have compressed peripheral nuclei appearing as though they are transformed giant cells. The surrounding tissue is infiltrated with plasma cells, lymphocytes and foam cells x 400.

formation of typical lesions. The mode of transmission is not known.

The disease may affect *any part of the skin* but has a predilection for the face, ears and extensor surfaces of the extremities. The lesions may be divided into a *nodular* and a *maculoanesthetic* type. The former arises either as papules which enlarge to nodules or is preceded by the formation of red or brownish red flat areas of discoloration. The nodules are single, sharply circumscribed and measure as much as 3 cm. in diameter or they coalesce to form conglomerate masses. They may then regress and disappear or produce ulcerations of the epidermis. *Histologically*, the lesions are found in the dermis or subdermis. Early they consist of a diffuse or a perivascular infiltration with lymphocytes and plasma cells. As they become older they tend to form tubercles of epithelioid cells surrounded by scattered plasma cells, lymphocytes and occasional giant cells. In the adjacent tissue there are foam cells and leprosy cells. The latter are large clear spaces containing aggregations of closely packed mycobacterium leprae which are known as globi

fluctuant, ulcerates and discharges viscid, yellow or brown pus onto the surrounding skin. As a result of this seeding, new cutaneous lesions are formed and the process repeats itself. Simultaneously, the original focus gives rise to a chain of secondary nodules and abscesses that are distributed along the course of the draining lymphatic channels. The *histologic* picture is not distinctive. The epidermis becomes hypertrophic and sends prolongations of regular epithelium into the corium. The latter exhibits large tubercles composed of a central area of necrosis, neutrophils and macrophages, a mid zone of epithelioid and Langhans' giant cells, and a peripheral

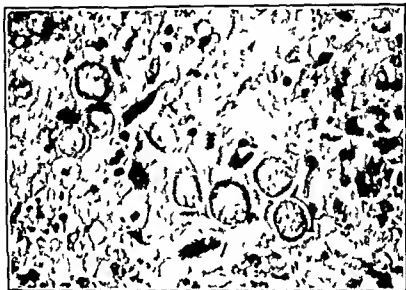


FIG. 21 — Coccidioidomycosis showing light spores composed of a doubly refractile rim and young ill-defined endospores. $\times 400$

zone of plasma cells, lymphocytes, blood vessels and connective tissue. Rarely, the sporotrichum can be found in histologic sections. It exists as a short, cigar-shaped, rod-like form that measures about 2×5 microns, and less often as an ovoid or spherical cell. Either of these may be found free or engulfed in macrophages or neutrophils. The *diagnosis* is made by *animal inoculation*. White male rats injected intraperitoneally with pus from the initial sore develop lesions in the peritoneum and testes. Smears of these reveal numerous organisms.

Coccidioidomycosis is a chronic granulomatous disease caused by *coccidioides immitis*. It may be primary in the skin but more often the cutaneous manifestations are only a part of a generalized dissemination. As a result the lesion may begin as papules or nodules within the skin proper, or as larger masses in the subcutaneous tissues. In either case as they enlarge they break down, caseate and ultimately discharge a thick, yellowish grey, viscid pus. The disease spreads by direct extension and by way of the lymphatics. *Histologically*, the epithelium becomes hyperplastic and sends branching extensions into the corium. Intraepidermal abscesses of plasma cells, neutrophils, lymphocytes, epithelioid cells and giant

latter consist of nuclear fragments, neutrophils, degenerating epidermal cells, epithelioid cells, Langhans' giant cells and the fungus cells. These are free or within giant cells and are present in the form of single or budding doubly refractile spores that measure about 14 microns in diameter (Fig. 19). The corium exhibits similar abscesses, well-formed tubercles of epithelioid cells, Langhans' giant cells and peripheral lymphocytes, and a diffuse infiltration with plasma cells and lymphocytes.

Actinomycosis of the skin usually arises as a direct extension from a more deeply situated lesion in the neck, the lungs or the cecum.

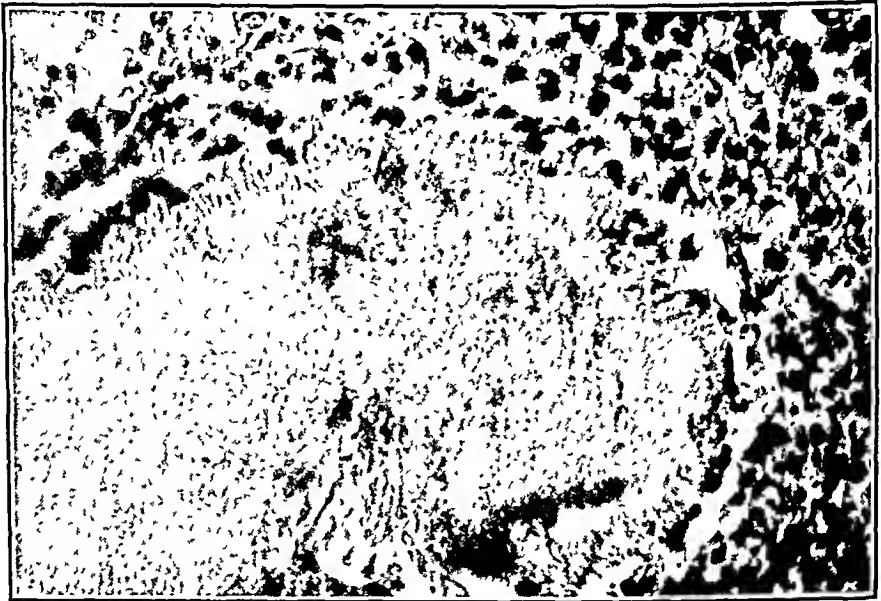


FIG. 20.—Actinomycosis illustrating a tangled colony of the fungus with clubbed shaped peripheral excrescences x 400.

As the large subcutaneous mass encroaches upon the skin the latter becomes tense and of a deep bluish red color. Perforations in the form of multiple sinus tracts, or a single large ulcer, are followed by a discharge of seropurulent or sanguineous pus. This contains variously colored *actinomycotic granules* measuring less than 1 mm. in diameter. They consist of a tangled central mass of gram positive mycelium at the periphery of which are numerous gram negative, clubbed shaped radiating, rods (Fig. 20). *Histologically*, the lesion is a granuloma whose most specific structure is the organism itself. It occupies the center of the nodule and is surrounded by lymphocytes, neutrophils, macrophages, plasma cells and young connective tissue cells. The supporting stroma is edematous and is diffusely infiltrated with neutrophils and plasma cells. Coalescence of the nodules produces an enlargement of the abscesses and burrowing intracutaneous sinus tracts. The end result is extensive scar formation.

Sporotrichosis is a chronic granulomatous disease that usually affects the upper extremities of farmers but may involve any part of the body. The initial lesion consists of a small *abscess* at the site of the trauma. This enlarges to form a *nodule* which becomes

varies with the age of the lesion and, accordingly, dermatologists have subdivided the disease into at least six types. Since the differences between these are only one of degree, they need not be considered separately. The most characteristic changes are in the epidermis (Fig. 23). The surface discloses patchy or layered parakeratosis, that is, both an increase in thickness of the corneum together with a retention of pyknotic nuclei. The stratum granulosum is decreased in thickness or entirely absent. The prickly cell layer is greatly hypertrophied and sends clubbed shaped, finger-like projections into the dermis. Neutrophils infiltrate the entire

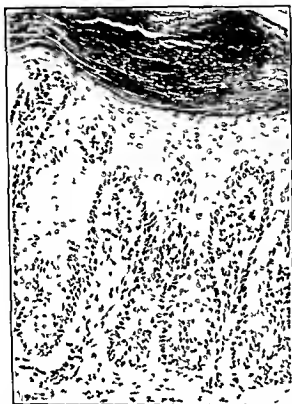


FIG. 23.—Psoriasis showing parakeratosis, intraepithelial abscess in the stratum corneum, hypertrophy of prickly cells forming club-shaped rete cones and enlarged papillae. $\times 100$.

epidermis and in the stratum corneum they collect to form micro-abscesses. At the same level there are also air spaces which account for both the grey appearance of the scales and the ease with which they are lifted off. As a result of the downward growth of the epidermis the papillae between the rete pegs become hypertrophied and clubbed shaped. They disclose an increase in tortuous capillaries, edema and a diffuse slight infiltration with lymphocytes. In the remainder of the corium there is less edema and a mild perivascular accumulation of lymphocytes and mononuclear cells.

Molluscum Contagiosum—*Molluscum contagiosum* is a chronic contagious disease caused by a virus and characterized by the formation of intraepithelial inclusions known as molluscum bodies.

cells are characteristically found. The corium is diffusely infiltrated with plasma cells and contains both miliary abscesses and tubercles that are indistinguishable from those in tuberculosis. The causative organism is easily found in smears of the pus and in histologic sections, where it is present both free and within giant cells (Fig. 21). In vivo it exists either as a single spore or as a sac filled with endospores. The spores measure from 5 to 30 microns in diameter and reveal a thick, smooth, doubly refractile, delimiting membrane.

Histoplasmosis is almost always a systemic disease which some-

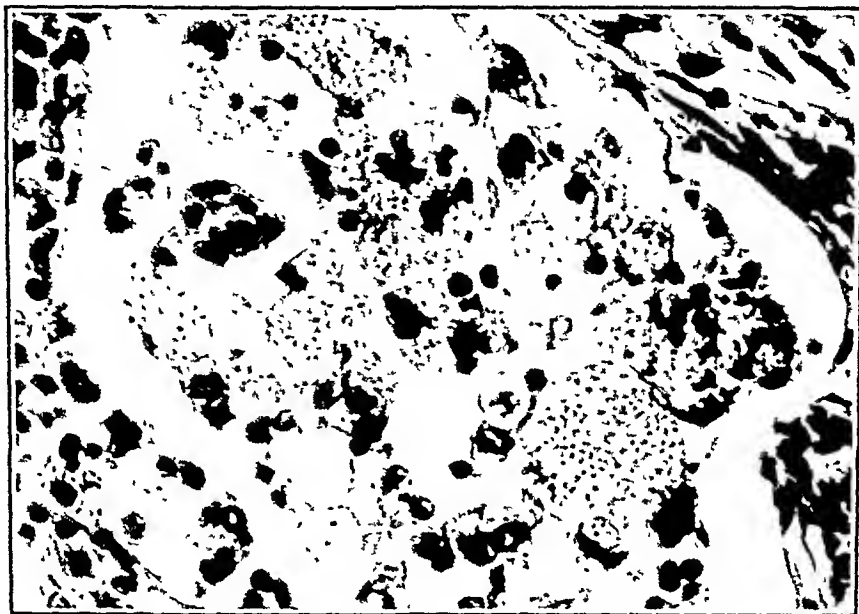


FIG. 22 —Histoplasmosis. Large phagocytes are filled with numerous small organisms x 400.

times is accompanied by lesions in the skin. It is caused by the *histoplasma capsulatum*. This is a round or oval organism measuring 2 to 4 microns in diameter (Fig. 22). It is surrounded by a doubly refractile rim and contains a clear cytoplasm in which the chromatin material is either clumped or diffusely scattered. The cutaneous sores exist as papules, nodules or thick infiltrates with ulcerating surfaces. *Histologically*, the lesion is a nodular granuloma. It is composed of a central area of necrosis, a middle zone of macrophages filled with histoplasma organisms and a peripheral infiltrate of plasma cells, lymphocytes and neutrophils. Giant cells of the Langhans' type may or may not be present.

Psoriasis.—Psoriasis is a chronic disease of the skin of unknown etiology that occurs on the extensor surfaces of the limbs, on the scalp and less frequently on other parts of the body. The lesions first appear as minute, pinhead sized, bright red papules. These gradually enlarge to form plaques and, particularly on the backs of the hands, warty excrescences. Simultaneously they become covered with pearly white, loosely attached scales which when removed leave fine points of hemorrhage. The *histologic* appearance

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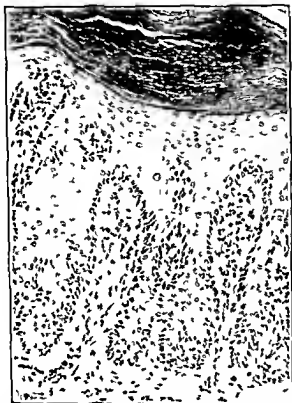


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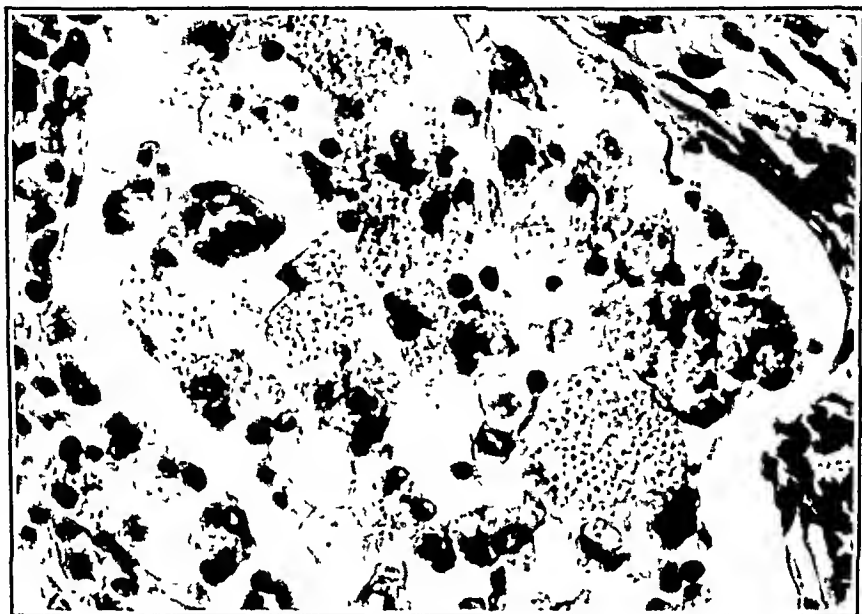


FIG 22 —Histoplasmosis. Large phagocytes are filled with numerous small organisms x 400

times is accompanied by lesions in the skin. It is caused by the *histoplasma capsulatum*. This is a round or oval organism measuring 2 to 4 microns in diameter (Fig. 22). It is surrounded by a doubly refractile rim and contains a clear cytoplasm in which the chromatin material is either clumped or diffusely scattered. The cutaneous sores exist as papules, nodules or thick infiltrates with ulcerating surfaces. *Histologically*, the lesion is a nodular granuloma. It is composed of a central area of necrosis, a middle zone of macrophages filled with histoplasma organisms and a peripheral infiltrate of plasma cells, lymphocytes and neutrophils. Giant cells of the Langhans' type may or may not be present.

Psoriasis.—Psoriasis is a chronic disease of the skin of unknown etiology that occurs on the extensor surfaces of the limbs, on the scalp and less frequently on other parts of the body. The lesions first appear as minute, pinhead sized, bright red papules. These gradually enlarge to form plaques and, particularly on the backs of the hands, warty excrescences. Simultaneously they become covered with pearly white, loosely attached scales which when removed leave fine points of hemorrhage. The *histologic* appearance

Tumors—Because of the complex anatomical composition of the skin, cutaneous tumor formations are extremely diverse. Virtually every histologic component may be responsible for an innocent or a malignant neoplasm. Thus from the epidermis proper there may arise a clavus, a papilloma, an epidermoid cyst or a carcinoma, from sebaceous glands a cyst, a hyperplasia, an adenoma or a carcinoma, from sweat glands a hydradenoma or hydradenoid carcinoma, from hair follicles (and probably sebaceous and sweat glands) epithelioma adenoides cysticum of Brooke, from connective tissue a fibroma, a fibrosarcoma, a myxoma and a myxosarcoma, from fat tissue a lipoma or a liposarcoma, from histiocytes, connective tissue or fat cells a xanthoma, from pigment producing cells (probably nervous in origin) a pigmented nevus or a melanoblastoma, from nerve tissue a neuroma, a neurofibroma or a neurofibrosarcoma, from vessels an angioma, Kaposi's sarcoma, or a lymphangioma, from vessels, nerves, connective tissue, and muscle tissue a glomal tumor, and from mesodermal and ectodermal elements a mixed tumor. In addition there are several tumors that are foreign to the skin or whose local origin is questioned. These include metastatic neoplasms, leukemias, Hodgkin's disease and mycosis fungoides. While this classification is not intended to be all inclusive it does encompass most of the ordinary lesions seen in the laboratory. Some of the conditions mentioned have already been discussed in the earlier part of this chapter. The salient features of the remaining lesions will now be considered.

Clavus—A clavus or corn is a localized painful hyperkeratosis of the epidermis. It is found at pressure points particularly on the feet and as such is located over the bony prominences of the toes and less often the soles. It is hard when situated on exposed surfaces, but it is soft when located in moist areas such as between the toes. *Histologically*, there is a conical, piled up mass of keratin, the apex of which is directed towards the corium, and frequently a complete atrophy of the subjacent epidermis proper. Pain results from pressure of the cone upon the nerve endings in the dermis.

Papilloma—A papilloma is a localized, elevated hyperplasia of the epithelium. It is found anywhere on the body but it is particularly common on the dorsal surface of the fingers and hands, where it is known as the *common wart* (*verruca vulgaris*), and around the anus, external genitals and thighs where it is known as the *venereal wart* (*condyloma acuminatum*). Because of the tendency to spontaneous regression, disappearance and recurrence it is questionable whether the lesion is a true neoplasm or whether it is of infectious or viral origin. *Grossly*, the nodule may be less than a millimeter or several centimeters in diameter, single or multiple, discrete or confluent, pedunculated or sessile, smooth or rough, firm or relatively soft, and grey to brown in color. *Histologically*, it consists of a thin or broad core of connective tissue covered with villi of hyperplastic epithelium (Fig. 25). Surface keratinization may be slight or marked. The broadened prickle cell layer frequently shows edema and prominent intercellular bridges and contains sharply circumscribed, homogeneously eosinophilic, round

The *lesions* are widely distributed over the body but have a predilection for the face, male genital organs and the inner surfaces of the thighs. They appear as collections of discrete or coalescing pink elevations that measure as much as 2 cm. in diameter. The surface is flat, centrally umbilicated and discharges spontaneously, or upon pressure, a cheesy, granular material. The *histologic* changes are confined to the epidermis. They consist of a marked hypertrophy of the prickle cell layer with downward prolongations of the rete cones and an elevation of the entire mass above the surface of the surrounding skin. The molluscum body starts in the

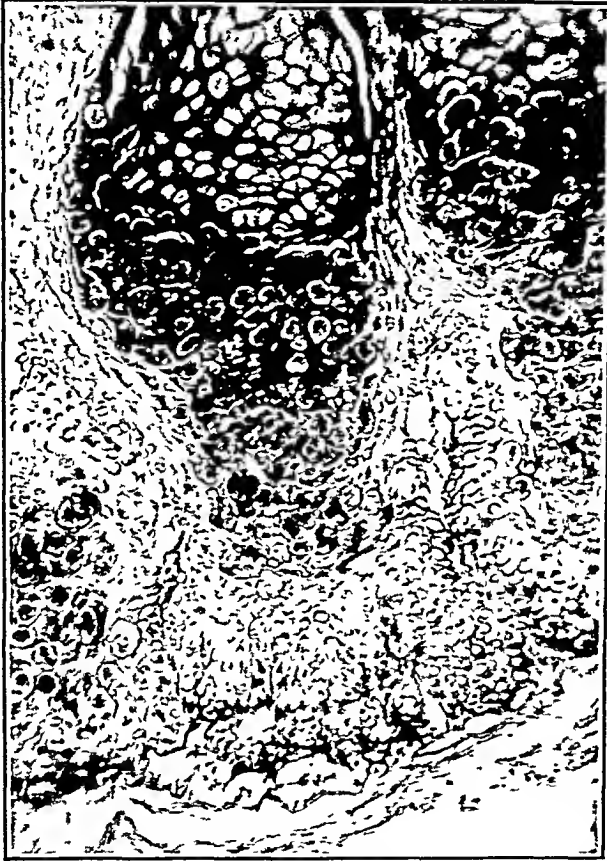


FIG. 24.—Molluscum contagiosum illustrating numerous intra-epithelial molluscum bodies in various stages of development. $\times 100$.

prickle cells that are located several rows above the basal layer (Fig. 24). Initially, there appears a clear non-staining vacuolated area in the vicinity of the nucleus, and the cytoplasm, which houses the elementary bodies, becomes coarsely granular. Gradually the granules condense to form a solid round, sharply demarcated, deeply eosinophilic mass. Simultaneously, the former nucleus of the epithelial cell becomes pycnotic, crescentic and pushed aside. As the bodies get older they gradually ascend to the surface. By the time they reach the corium they are cornified, surrounded by a clear space, often stain blue instead of eosinophilic, and in many instances completely lose the pycnotic nucleus. There are no noteworthy changes in the corium.

Tumors—Because of the complex anatomical composition of the skin, cutaneous tumor formations are extremely diverse. Virtually every histologic component may be responsible for an innocent or a malignant neoplasm. Thus from the epidermis proper there may arise a *clavus*, a *papilloma*, an *epidermoid cyst* or a *carcinoma*, from sebaceous glands a *cyst*, a *hyperplasia*, an *adenoma* or a *carcinoma*, from sweat glands a *hydradenoma* or *hydradenoid carcinoma*, from hair follicles (and probably sebaceous and sweat glands) *epithelioma adenoides cysticum* of Brooke, from connective tissue a *fibroma*, a *fibrosarcoma*, a *myxoma* and a *myxosarcoma*, from fat tissue a *lipoma* or a *liposarcoma*, from histiocytes, connective tissue or fat cells a *xanthoma*, from pigment producing cells (probably nervous in origin) a *pigmented nevus* or a *melanoblastoma*, from nerve tissue a *neuroma*, a *neurofibroma* or a *neurofibrosarcoma*, from vessels an *angioma*, *Kaposi's sarcoma*, or a *lymphangioma*, from vessels, nerves, connective tissue, and muscle tissue a *glomus tumor*, and from mesodermal and ectodermal elements a *mixed tumor*. In addition there are several tumors that are foreign to the skin or whose local origin is questioned. These include metastatic neoplasms, leukemias, Hodgkin's disease and *mycosis fungoides*. While this classification is not intended to be all inclusive it does encompass most of the ordinary lesions seen in the laboratory. Some of the conditions mentioned have already been discussed in the earlier part of this chapter. The salient features of the remaining lesions will now be considered.

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bodies known as Russell's bodies. The rete pegs are usually hyperplastic but are regular. Sometimes the basal cell layer contains an abundant amount of brown pigment which gives the papilloma a brown color. This should not be confused with a pigmented nevus which, as has already been seen, consists primarily of melanoblasts located in the dermis. Except for an inflammatory reaction and an increased vascular supply the underlying corium shows no noteworthy changes. A *cancerous transformation* in a



FIG. 25.—Papilloma. A thin core of connective tissue is covered with hyperplastic stratified squamous epithelium. x 100.

benign papilloma while very rare does occur and is manifest by an irregular proliferation of epidermal cells that invade the adjacent dermis.

Epidermoid Cysts.—In addition to the *congenital* midline epithelial cysts already considered, epidermoid cysts may develop as a result of *trauma*. This is accomplished either by implantation of the surface epithelium into the dermis or by causing it to proliferate. Although rare, such cysts are found on the hands of laborers and in post-operative scars. Histologically they are indistinguishable from sebaceous cysts.

Carcinoma.—Carcinoma of the skin is a common disease in people beyond the age of fifty-five years. It affects men more often than women and the white race seven times as frequently as the colored. It is located on all parts of the body but is particularly common on the exposed surfaces as the ears, face and hands where it is frequently associated with senile keratosis. The ultimate *cause* of cutaneous carcinoma is, of course, not known but the predisposing causes are numerous. These may be conveniently divided into (1) physical agents and (2) chemicals. Physical agents which are known to cause carcinoma of the skin include ultraviolet rays (sunlight), roentgen rays, other radioactive elements and continued

chronic irritation. Among others, examples of the latter are found in the mouth, and, in kangri users, in the skin of the abdominal wall.

The relation of single or, for that matter, even of repeated trauma to carcinoma is extremely important from the standpoint of compensation but unfortunately cannot be settled. It is doubtful whether there is any relation between the two unless trauma first produces a scar, for it is known that about one fifth of the carcinomas of the scalp, trunk or legs develop in pre-existing scars caused by burns, surgical operations, lacerations and ulcerations. Shields Warren has suggested the following criteria for incriminating trauma as the cause of a malignant neoplasm (1) integrity of the tumor site prior to the injury (2) disruption of the continuity of the tissue at the site of the trauma (3) reasonable interval of time between the injury and the development of the tumor and (4) the tumor must be of a type that would result from regeneration and repair of the injured tissue. Some of the chemicals which have been considered to cause carcinoma are arsenic, chromates, nickel carbonyl, pitch, tar, soot, anthracene oil and the aniline dyes. Three types of carcinoma of the epidermis that will be considered here are squamous cell, basal cell and Bowen's disease.

Squamous cell carcinoma occurs four times as often in men as it does in women and involves in order of frequency the lower lip, nose, ears, genitals, neck and extremities. The lesion starts in one or several widely scattered areas as a small papule or nodule that rapidly enlarges and soon ulcerates (Fig. 26). The edges of the



FIG. 26.—Squamous cell carcinoma. The lesion is raised firm and centrally ulcerated. The surrounding skin reveals sunken keratosis.

ulcer are raised firm and pink to grey. The floor is covered with necrotic grey tissue and exudate, and the base is composed of a firm mass of grey to white tissue that rapidly infiltrates the adjoining structures. The entire mass is fairly well delineated but is not encapsulated. *Histologically*, the tumor is seen to originate in the basal cells of the epidermis which, however, differentiate to form prickly cells (Fig. 27). The neoplastic downgrowths from the epidermis are seen as branching columns and nests of irregular cells that unhesitatingly infiltrate through and beyond the corium. In the more slowly growing and better differentiated lesions the cells resemble closely the prickly cells of normal epithelium. They are

polygonal, large, sharply defined, have an abundant amount of pink cytoplasm and relatively large deeply stained nuclei. Intercellular bridges may or may not be seen. The cells in the center of the masses have a tendency to undergo keratinization and as such become crescentic and closely packed together in whorls to form characteristic pearls. In somewhat more rapidly growing tumors the cells, still arranged in cords or nests, are less well differentiated. They are less distinct, smaller, more elongated and have only a moderate amount of ill defined pink staining cytoplasm. The nuclei are round, oval or even spindle shaped, and reveal considerable

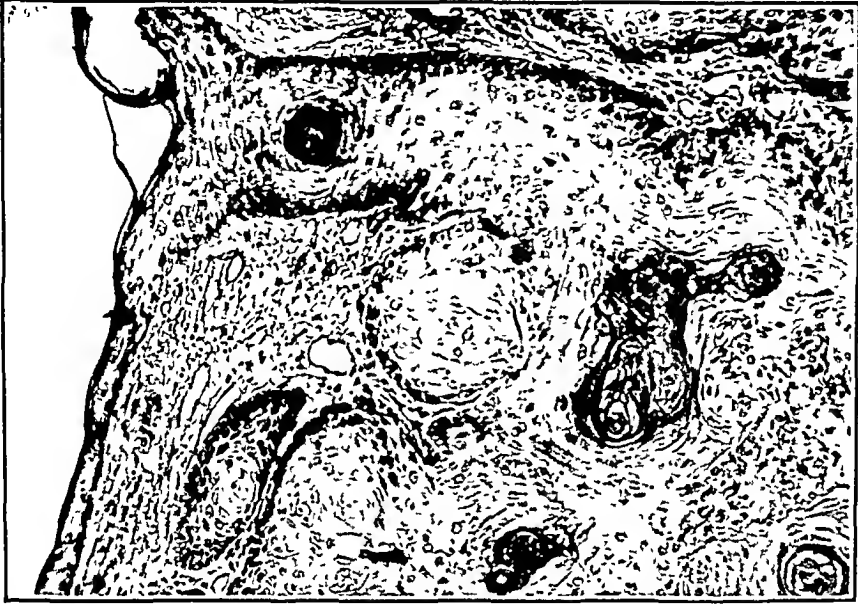


FIG. 27 —Well-differentiated squamous cell carcinoma showing cords of prickle cells with well-formed pearls invading the corium from the epidermis x 100.

hyperchromatism and numerous mitotic figures. There are no pearls. In very actively growing tumors the cords and nests are replaced by a diffuse infiltration of single cells that often lose all resemblance to the parent tissue. They are round, oval, polygonal or irregular, have a varied amount of cytoplasm, and bizarre, extremely hyperchromatic often multinucleated nuclei. The stroma in squamous cell carcinoma is usually abundant, fibrous and densely infiltrated with plasma cells and lymphocytes.

Following *Broders' classification* it has become customary to grade squamous cell carcinoma from one to four. Grade one represents well differentiated tumors that do not deviate a great deal from normal appearing epidermis and grade four represents highly anaplastic growths that have lost all semblance to squamous epithelium. Grade two and three are in between. While in general such distinctions are of value, they must be interpreted in conjunction with the rapidity of growth of the tumor, its location and the presence or absence of metastases. The *diagnosis* of carcinoma is fostered when any indurated ulcer fails to heal under proper treatment, and it is readily confirmed by histologic examination.

Treatment of squamous cell carcinoma of the skin is either surgical excision or irradiation therapy. Each is highly effective if the lesion is seen early and if treatment is adequate the first time. There is no reason why every case of carcinoma of the skin should not be cured. Unfortunately prognostication on the part of the physician and the patient coupled with inadequate or improper therapy too often result in catastrophe. Squamous cell carcinoma spreads by local extension, by lymphatics and by the blood stream. In 16 per cent of cases there is already metastasis to the regional lymph nodes when the patient is first seen. The prognosis depends on the size and location of the tumor and upon the presence or absence of metastases.

Basal cell carcinoma is likewise found more often in men than in women, occurs in a slightly younger age group than does squamous cell carcinoma, and has a predilection for the upper part of the face, the nose and the ears. Grossly, the lesion may appear as an ulcer, a papule or a nodule (Fig. 28). The ulcer starts as a pale red area

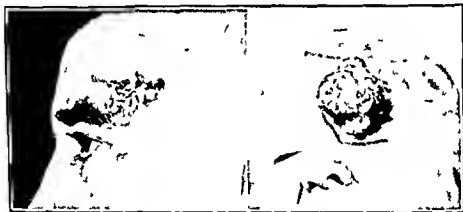


FIG. 28

FIG. 29

FIG. 28—Ulcerating basal cell carcinoma. The edges are irregular but sharp and not raised.

FIG. 29—Pedunculated cystic basal cell carcinoma.

with but slight induration of the dermis. Gradually the surface becomes roughened, then scaly and finally the crust falls away leaving an underlying ulcer. The edges of the latter are usually level with the skin or only slightly elevated. They are sharp, smooth, firm and pink to grey. The lesion enlarges by gnawing away at the adjacent tissue until, if let go long enough, the entire nose, ear or side of the face is eaten away (rodent ulcer). The papular lesions enlarge to become nodules that measure as much as 6 cm. in diameter. The latter are pedunculated or sessile, smooth or rough, often superficially ulcerated, pink to grey and frequently transparent (Fig. 29). Unlike the primarily ulcerating lesions these tumors are usually confined to the outer portions of the dermis and do not extend into the subcutaneous tissue. Histologically, basal cell carcinoma usually arises from the basal cells of the epidermis and less often from the sebaceous glands and hair follicles. If sections are made at the right level, cords and nests of epithelial

cells are seen to stream from the basal layer into the corium (Fig. 30). Here they arborize to form branching structures with bulbous ends. Except for being more heavily stained the cells are similar to the basal cells of the epidermis. In the center of the strands they are crowded, have a moderate amount of ill-defined cytoplasm and round or oval, evenly stained nuclei. At the periphery of the masses they are slightly larger, more deeply stained, have almost a columnar appearance and are arranged at right angles to the main mass. Usually the cords and nests are solid but sometimes the cells in the center undergo degeneration to form pseudoglandular or cystic



FIG 30 —Basal cell carcinoma showing solid nests of basal cells infiltrating the corium. x 100

spaces filled with blue staining, mucoid material (Fig. 31). The surrounding stroma is fibrous and, when the tumor ulcerates, it is diffusely infiltrated with plasma cells and lymphocytes.

A *diagnosis* of basal cell carcinoma can often be made from the gross appearance of the lesion in conjunction with a history of long duration. In carcinoma of the skin it is the size of the lesion that prompts the patient to seek medical aid and not its duration. Consequently patients with basal cell carcinoma state that the lesion has been present for months or years whereas those with squamous cell carcinoma speak in terms of weeks or months. A clinical impression, nevertheless should always be varified by histologic examination of a piece of tissue. *Treatment* is either surgical excision or irradiation and, as in squamous cell carcinoma, it should be adequate the first time. Under such circumstances, the *prognosis* is excellent for basal cell carcinoma does not metastasize.

Squamo-basal cell carcinoma is a term reserved for lesions which histologically have the appearance both of squamous cell carcinoma and of basal cell carcinoma and are typical of neither one nor the other.

Bowen's disease is a chronic, originally described as a piceancerous, disease that occurs on all parts of the body, affects both sexes with equal frequency and lasts twenty to thirty years. The lesions are single or multiple, papular or nodular, light red in color, and reveal a rough, horny or superficially ulcerated surface which is covered with a crust. Removal of the latter leaves an oozing, granular shallow ulcer. Sometimes the lesions are plaque-like, extend at the periphery and simultaneously tend to heal in the center. *Histologically*, the changes are those of carcinoma in situ—an epidermoid carcinoma that remains localized to the epithelium (Fig. 32). There

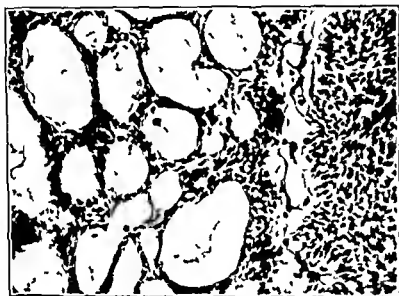


Fig. 31—Cystic basal cell carcinoma illustrating pseudolands filled with basophilic mucoid material. $\times 200$

are keratosis and parakeratosis (keratosis with retention of pyknotic nuclei), hyperplasia of the prickle cell layer, and proliferation and extension of the rete cones into the dermis. The most striking change, perhaps, is the disorderly arrangement of the prickle cells. Their polarity is completely lost. They vary considerably in shape and size and show edema and vacuolization of the cytoplasm. The nuclei are pyknotic and pushed aside, or are large, hyperchromatic and frequently in a state of mitosis. Sometimes several are grouped together in a single cell. Occasionally there is a coalescence and an attempt at keratinization of a group of prickle cells to produce structures resembling ordinary pearls. The lesion, although confined to the epidermis for years, may at any time break through the basal layer and not only infiltrate the dermis but metastasize widely. Histologically the infiltrating and metastasizing tumors are typical squamous cell carcinomas. The diagnosis is made from the gross appearance but should always be confirmed histologically. The treatment is surgical excision.

Sebaceous cysts may be found anywhere in the skin where there are sebaceous glands and this, as has been seen, includes all areas

except the palms and soles. They are particularly common on the scalp where they are known by the laity as "wens." The *cause* is a congenital or an acquired obstruction of the mouth of a gland with retention of secretion and consequent distention of the gland proper. *Grossly*, they are seen as small, round, not tender, intracutaneous nodules that usually measure up to 2 cm. but sometimes to 5 cm. in diameter. The smaller ones are quite firm and shotty but the larger ones are softer and putty-like in consistency. The covering epidermis is usually intact. Larger tumors, however, have a tendency to break down and discharge a yellowish grey, greasy flake-like or

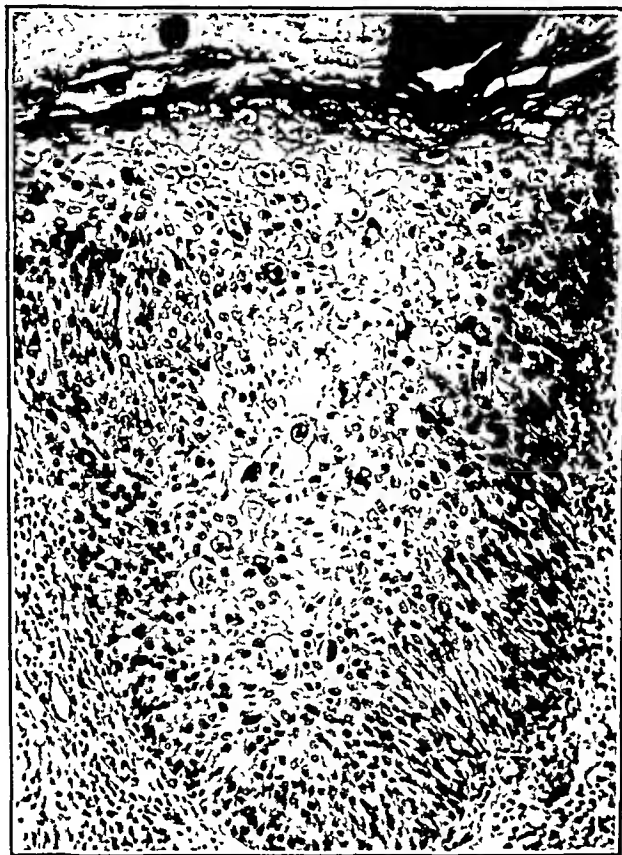


FIG. 32 —Bowen's disease (carcinoma in situ) showing hyperkeratosis, marked hypertrophy of the rete cones and a disorderly arrangement of irregular prickle cells x 100.

cheesy material. When a small lesion is examined microscopically its connection with a hair shaft or surface epithelium may be evident but usually, as a result of growth and other changes, the point of origin can not be identified. *Histologically*, the lining of the cyst consists of a flat attenuated or a broad hyperplastic membrane of stratified squamous epithelium the keratinizing surface of which is directed toward the lumen (Fig. 33). The cyst is filled with sebaceous material that arises as a degeneration of sloughed cells, and may sometimes contain giant cells of the foreign body type. Sebaceous cysts may become infected, calcified or undergo a cancerous change. The latter occurs in about 4 per cent of cases. The *treatment* is surgical excision.

Sebaceous adenoma and hyperplasia are practically indistinguishable. Each consists of an increase in number and size of the glands with the formation of solitary or multiple intracutaneous nodules of varying dimensions. The best and most common example of their hypertrophy and hyperplasia is *rhinophyma*, also known as whisky or rum nose. It is an irregular bulbous enlargement of the lower half of the nose that usually occurs in men over the age of fifty years. Microscopic examination reveals a normal or atrophic epidermis, enlarged gaping follicles filled with keratin and sebum, and numerous hypertrophied and hyperplastic sebaceous glands that open into the

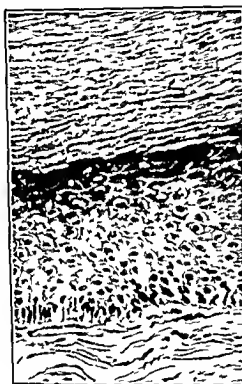


FIG 33

FIG 33—Sebaceous cyst. The lining is composed of stratified squamous epithelium which is covered with a thick layer of keratin. $\times 200$



FIG 34

FIG 34—Rhinophyma showing an enlarged gaping follicle filled with keratin and greatly hypertrophied sebaceous glands. $\times 75$

dilated ends of the hair follicles (Fig 34). Their cells are regular but larger than normal. The supporting stroma is fibrous, frequently infiltrated with plasma cells and lymphocytes, and may or may not contain an excessive supply of blood and lymph vessels. Treatment, if desired, consists of shaving off the excess tissue to the level of the nose.

Carcinoma of sebaceous glands is not a common tumor. Some authors give the incidence as high as 4.6 per cent of all cutaneous neoplasms, but Warren and Warren saw only 29 cases in 4000 cutaneous carcinomas. The tumor is found beyond middle life, affects both sexes with equal frequency, and is located most often on the eyelids, face and scalp. The lesion starts in the deeper

portions of the dermis as a sharply circumscribed, firm often yellowish nodule. It grows very slowly, ulcerates late, infiltrates the adjoining tissue, and in time produces local and widespread metastases. *Microscopically*, the degree of differentiation varies from tumors that closely resemble normal sebaceous glands to anaplastic growths in which careful search is necessary to identify foci of sebaceous cells. The former are composed of large polyhedral cells with distinct boundaries, lightly stained granular or vacuolated cytoplasm, and evenly stained fairly large nuclei. They differ from normal sebaceous glands in that the flat peripheral cells are absent and in that the external layer of cells is more basophilic. The more anaplastic tumors infiltrate the surrounding tissue in the form of nests and strands, show considerable variation in shape and size of the cells, reveal more granularity, less vacuolization and sometimes keratinization of the cytoplasm, and disclose hyperchromatism and irregularity of the nuclei. Mitoses are frequent. *Treatment* of sebaceous carcinoma is wide surgical excision. *Recurrences* are common.

Sweat gland tumors.—The literature on tumors of the sweat glands is confused to say the least. For all practical purposes there seems to be little justification in subdividing the lesion into numerous categories and attaching unwieldy names to each. In this section only two types of tumors will be recognized—a benign one called a hydradenoma and a cancerous one called a hydradenoid carcinoma.

Hydradenomas are single or multiple, elevated, papillary, pedunculated or intradermal and subcutaneous nodules that measure from 1 to 4 cm. in diameter. They are smooth, rarely ulcerated, sometimes translucent and are found on all parts of the body wherever there are sweat glands. *Histologically*, they may arise from and resemble either the ducts or the glands. The epithelial groups may be clustered together or more frequently scattered throughout the corium. They exist as solid cords or masses, as small glands, as dilated cystic spaces with or without papillary infoldings, as drawn out slit-like structures similar to intracanalicular fibroadenoma of the breast, or as large alveolar spaces. About the periphery the masses may or may not contain myoepithelium. The *solid nests* are composed of closely packed cells that bear some resemblance to basal cells, squamous cells and even sebaceous cells. They are round or polygonal, of varying dimensions, and contain a scanty or abundant reticulated cytoplasm and medium sized dense nuclei. The cells in tumors forming *small glands* are quite similar to those lining normal glands except that they are several layers deep, are less regular, have indistinct margins, clear cytoplasm and deeply stained nuclei. The cells in lesions forming cysts, papillae and alveoli are usually cuboidal or tall columnar, have a varied amount of faint blue, colorless or intensely eosinophilic cytoplasm and deeply stained central or basilar nuclei (Fig. 35). The cystic spaces may contain hyalin, granular or horny material. About the periphery of the adenomas there are often remains of normal sweat glands and ducts. The *diagnosis* is sometimes quite difficult. The *treatment* of hydradenoma is surgical excision.

Hydradenoid carcinoma is an uncommon cancer that probably originates in a previously benign adenoma. Most patients have a tumor for thirty years or more and then at the age of sixty years or beyond it begins to grow and invade the surrounding structures. Occasionally, however, it is of short duration. The criteria necessary for a diagnosis of hydradenoid carcinoma have not been clearly defined. It appears as though they may closely resemble the benign growths, except that they infiltrate and destroy the adjoining structures, or that they may in part or wholly resemble basal or



FIG. 35—Hydradenoma from an axilla illustrating papillae of large columnar cells with intensely eosinophilic cytoplasm and relatively small round nuclei. $\times 200$

squamous cell carcinoma. The treatment is surgical excision. A few lesions recur and an occasional one metastasizes.

Epithelioma adenoides cysticum of Brooke is a term reserved by some, for multiple, benign, hereditary nodules that occur about the face at the age of puberty and that arise from the hair follicles, sweat glands and sebaceous glands. Other writers include under this caption any tumor composed of basal cells with cystic degeneration that arises from either the epidermis, hair follicles, sweat glands or sebaceous glands. Most of the lesions in the latter group occur about the eyelids, nose and face in people beyond middle age. They are indistinguishable both grossly and histologically from cystic basal cell carcinoma which has already been considered.

Fibromas are benign tumors of fibroblasts that may arise wherever there is connective tissue. In the skin they appear most often on the face and trunk as intracutaneous, elevated, sessile, or pedunculated nodules or masses of varying sizes. They are soft or firm and not tender. Histologically, soft fibromas are quite cellular, that is, they are composed of crowded spindle or oval cells with a moderate, or scanty amount of ill-defined, light pink staining cytoplasm. They are usually located in the outer portion of the dermis, are

sharply defined and as they grow they stretch and attenuate the overlying epidermis. Hard fibromas are essentially similar except that they contain fewer nuclei that are set in course, intertwining, collagen bundles (Fig 36).

Fibrosarcoma is the malignant counterpart of fibroma and like the latter it arises wherever there is connective or fibrous tissue. Its incidence in the skin is about 1 in 3000 surgical specimens examined in the laboratory. It is about as frequent as cutaneous fibroma. It affects the white race more often than the colored, two men to every woman, and is about equally distributed between the ages of

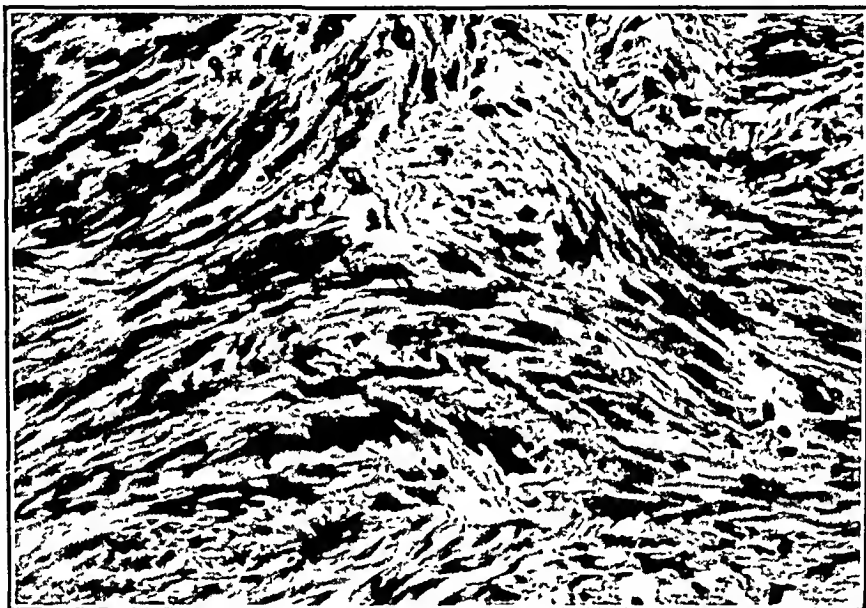


FIG 36 —Fibroma showing intertwining bundles of collagenous fibrous tissue x 200.

ten and seventy years. *Symptoms* consist of a rapidly growing painless swelling of a few weeks duration or of a sudden increase in size of a tumor that has been present for thirty years or more. Although trauma has often been considered as the initiating factor the cause of fibrosarcoma remains obscure. The tumor arises most often in the subcutaneous tissue and less often in the fascia, tendons, muscle and dermis itself. The *sites* in decreasing order of frequency are the upper thigh, shoulder, knee, elbow and other areas. By the time the patient is first seen the *neoplasms* are usually 5 cm. or more in diameter. They are firm or quite soft, sharply circumscribed, surrounded by a false capsule of compressed tissue, are often seen to engulf blood vessels, nerves, tendons or muscles, erode adjacent bones and produce pressure necrosis and ulceration of the overlying skin. Cut surfaces are composed of white, grey, solid, gelatinous or even cystic tumor tissue through which course fibrous septa and blood vessels (Fig 37). Foci of necrosis and hemorrhage are sometimes seen. The *histologic* appearance varies from highly cellular tumors that are indistinguishable from cellular fibromas to completely anaplastic growths. The cells are spindle, oval or sometimes round (Fig. 38). They contain a moderate or a scanty amount of

light pink or fibrillary cytoplasm. The nuclei are deeply stained, spindle, oval, less often round and sometimes quite bizarre. Fre-



FIG 37—Fibrosarcoma. The tissue is soft grey encephaloid and contains several areas of hemorrhage and necrosis.

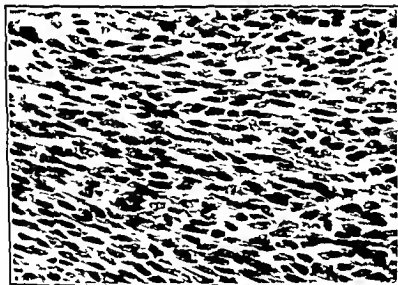


FIG 38—Fibrosarcoma. The cells are oval or spindle; the cytoplasm is scanty, and the nuclei are deeply stained and numerous. x 400

quently several are piled up within a single cell to form large irregular giant cells. Mitoses may or may not be numerous. When necrosis is present the viable cells are often grouped around blood

vessels to form solid perivascular collars. Fibrosarcoma *spreads* by local extension and metastasis. Metastasis by blood and lymph vessels usually occurs late in the disease or only after several recurrences. The chances of cure, therefore, are good provided the lesion is *widely excised* the first time. Unfortunately the localized nature of the growth coupled with the surgeon's desire to retain all function of surrounding muscles too often leads to incomplete removal or removals, recurrences, metastases and death. If the lesion is on an extremity and is large or inaccessible, or if it recurs after an apparently adequate local excision, amputation or dis-



FIG 39 —Myxoma A bulky tumor composed of grey somewhat gelatinous tissue

articulation should be performed. Irradiation has no effect. The *death rate* is about 70 per cent.

Myxoma is a benign tumor composed of embryonal connective tissue. It arises either as a primary lesion of connective tissue or as a degeneration of a fibroma, lipoma or chondroma. It is often, however, impossible to arrive at a histogenetic classification for by the time the tumor is examined its point of origin is no longer demonstrable. The *neoplasms* are commonly found in the loose subcutaneous tissue where they produce bulky, ill-defined, soft, gelatinous masses that insinuate themselves between the muscles, tendons, blood vessels, and nerves (Fig. 39). *Histologically*, they are composed of stellate cells with long drawn out, cytoplasmic processes (Fig. 40). The cytoplasm is otherwise moderate or scanty, and the nuclei are round or oval and evenly stained. Between the cells there is a scanty or an abundant amount of stringy, bluish stained, mucoid material and edema fluid. In addition, the tumors usually contain a varied number of spindle cells with spindle nuclei, and when an origin in a fibroma, lipoma or chondroma is demonstrable they exhibit remains of each of these neoplasms

The transition between a myxoma and a myxosarcoma is very subtle so that it is difficult to know exactly when to designate a tumor, one or the other. In general, however, when the lesion is cellular, when the individual cells show considerable variation in size and configuration, and particularly when bizarre giant cells are present a diagnosis of myxosarcoma is justified. In either case the tumors infiltrate locally but rarely metastasize. The treatment is wide excision or, if the tumors are bulky, located in the extremities, and have destroyed bone, amputation is indicated. Because of a lack of encapsulation and incomplete local removal recurrences are

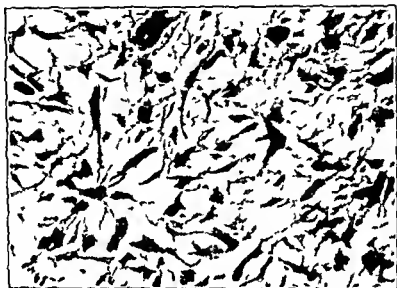


FIG. 40.—Myxoma showing elongated stellate cells separated by abundant basophilic ground substance or vacuoles. $\times 400$

common. The prognosis depends entirely on the site of the lesion and the structures involved. If the tumor can be completely excised or if in involved extremity can be amputated the chances of cure are good. Otherwise, the prognosis is poor.

Lipomas are benign tumors of fat cells that are commonly found in the subcutaneous tissue, between the muscles and in the viscera. The former may be found in any area of the body but are most frequent on the back of the neck, the forearm, the popliteal space and the axilla. They constitute about 5 per cent of all benign tumors, are found in 3 women to every man, and involve the white race more often than the colored. Ordinarily, the tumors make their appearance beyond the age of forty years when the body has a tendency to show accumulations of fat, but sometimes the lesions are present at birth. The latter are usually confined to one limb, are diffuse, reveal a stovepipe type of distribution and increase in size with growth of the body. They may be associated with a diffuse hemangioma and a hypertrophy of the muscles and bones of the involved extremity. *Acquired* lipomas are more circumscribed tumors that may be single or multiple. The latter are often irregularly distributed but sometimes they are remarkably sym-

metrical and are then easily confused with neurofibromatosis. The tumors vary in size from a few millimeters to many centimeters, may be flat, sessile or pedunculated, and are relatively soft in consistency. Usually they are confined by a thin connective tissue capsule, but sometimes they have no sharp line of delineation. Cut surfaces of smaller tumors show solid, moist or dry, light yellow fat tissue. Those of larger tumors are often lobulated and, in addition, reveal cysts filled with brown fluid and areas of myxomatous degeneration. *Microscopic* sections disclose adult fat cells with scanty intercellular connective tissue. Sometimes there are also foci of large polyhedral cells with sharp borders and granular cytoplasm that are called xanthoma cells. Lipomas grow locally and may cause death by pressure upon vital structures but they do not metastasize. The *treatment* is surgical excision. The *prognosis* is excellent.

Liposarcoma is a malignant tumor composed primarily of lipoblasts. It is reported as a rare tumor but its incidence is probably greater than generally supposed for in our own laboratory in the last two years we have seen 12 cases. Unlike lipoma, liposarcoma affects both sexes with equal frequency and, like its benign counter-

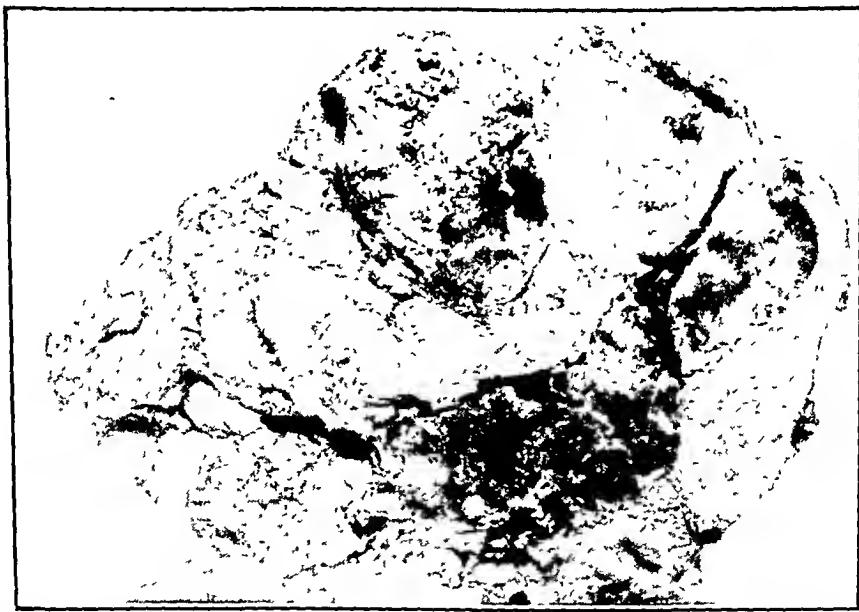


FIG 41 —Liposarcoma The surface is typically variegated and traversed by bands of fibrous tissue

part, it is found most often after the age of forty years. The duration of the tumor varies from a few months to many years. Its *locations* in approximately the decreasing order of frequency are retroperitoneal tissue, thigh, popliteal fossa, gluteal region, trunk, groin, leg, arm and most other areas of the body.

The *lesion* is usually single but may be multiple and presents as a large, bulky, nodular, moderately firm tumor that weighs as much as 69 pounds. Ordinarily it is well encapsulated, but sometimes the capsule is broken and it infiltrates the adjoining structures. Cut surfaces almost always disclose a variegated appearance (Fig. 41).

They are usually traversed by irregular bands of fibrous tissue. They may be solid, myxomatous or cystic, and range in color from that of normal fat to creamy, orange, red or even black (due to old hemorrhage). The histologic picture varies considerably from tumor to tumor and, indeed, in different areas of the same tumor. The cells that may be encountered are lipoblasts, lipocytes, very irregular and bizarre often multinucleated tumor cells, large foam cells, myxomatous connective tissue cells, large spindle fibrosarcomatous-like cells and phagocytes containing ingested hemosiderin (Fig 42). *Lipoblasts* are related to and derived from reticulum

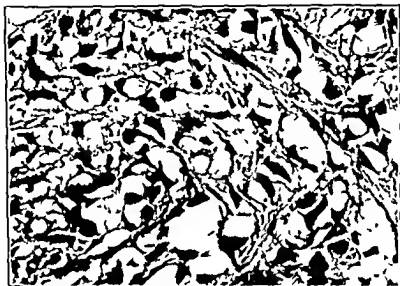


FIG 42—Liposarcoma. There are present a few lipoblasts and numerous more mature lipocytic tumor cells. $\times 400$

cells. Normally they are found among other places, in small foci in the periadrenal and perirenal fat tissue and in the bone marrow, although in the latter they are more difficult to identify. Both in normal locations and in tumors they exist as round oblong or slightly irregular cells, about the size of plasma cells, that contain an abundant amount of deeply eosinophilic cytoplasm and round deeply but evenly stained central or eccentric nuclei. In tumors they are often arranged in cords or nests that bear a superficial resemblance to adrenal or hepatic tissue. *Lipocytes* are ordinary vacuolated adult fat cells with peripherally crowded, crescentic nuclei. They are abundant in slowly growing tumors and, conversely, they are scanty or even entirely absent in rapidly growing ones. Aside from the primitive and fully differentiated cells the highly malignant growths show a *pleomorphism* of neoplastic fat cells that almost parallels that of osteogenic sarcoma. They are of all shapes and sizes, have a varied amount of eosinophilic or basophilic homogeneous, granular or vacuolated cytoplasm, and contain extremely irregular, hyperchromatic single or multiple nuclei. Foam cells are sometimes abundant, but at other times are

sparse. They are round, polygonal, sharply defined and disclose reticulated cytoplasm. Their nuclei are usually round evenly stained and relatively small. Some tumors show in addition, or almost exclusively, areas of stellate cells identical with those observed in a myxoma, and others are composed in part of large, intertwining, spindle cells that are similar to the cells seen in a fibrosarcoma. No matter how irregular the cells may be, there are always present in some portion of the tumor structures that can be identified as lipoblasts, lipocytes or at least lipocytic cells. They are best recognized by staining with any one of the fat stains. It should be emphasized, however, that in the more undifferentiated tumors only a few of the cells may disclose cytoplasmic fat droplets. The stroma in liposarcoma is usually scanty and quite vascular. Rupture of thin walled capillaries is frequent and accounts for the recent and old hemorrhage which is so commonly seen.

Liposarcoma *extends* locally and, after an interval of a few months to many years has a tendency to metastasize to distant organs, especially the lungs and the liver. The *treatment* is wide local excision. Failing this, if the lesion is located in an extremity, amputation should be performed. In tumors that are surgically inaccessible, or in small metastatic and recurrent foci, irradiation therapy is worthy of trial for there are some liposarcomas that are radiosensitive. The *prognosis* depends upon the location and size of the tumor and upon the presence or absence of metastases. Generally speaking it is not good.

Xanthomas are intradermal accumulations of foam cells that present a yellow to orange appearance. Some of the lesions are true tumors but others are nothing more than accumulations of lipid material in connective tissue, fat or reticuloendothelial cells. This is evidenced by the frequency with which such deposits are found in general diseases of lipid metabolism such as Hand-Schüller-Christian syndrome, Niemann-Pick's disease and Gaucher's disease, and the rapidity with which some lesions disappear when diets are restricted and the blood lipid levels are corrected. There are many clinical classifications of cutaneous xanthomatosis which, however, are not distinctive pathologically. The lesions may be congenital in origin, but more commonly they are found in adults after the age of forty years. Blood fatty acids, total lipoids and cholesterol may be normal, subnormal, or elevated. Accumulations of lipoids may be found anywhere in the skin but are most often located in the eyelids, and extensor surfaces of the elbows, heels and hands.

Grossly, the lesions may be flat, papular, or nodular and usually measure a few millimeters to less than a centimeter in diameter. Their color is brownish yellow or orange and they are almost always limited to the dermis. The *structure* varies according to the age of the deposits. In early xanthomas there are many round, oval, or polygonal foam cells with distinct outlines, reticulated or granular cytoplasm that takes a positive stain for fat or fatty material, and relatively small round evenly stained nuclei (Fig. 43). Coursing between these cells there is a scanty stroma of connective tissue

which is usually rich in capillaries. Multinucleated giant cells are sometimes quite numerous but at other times are in abeyance. As the lesions become older or involute, foam cells tend to disappear, lipoids are found extracellularly, there is an accumulation of hemosiderin, and fibrous tissue elements become quite conspicuous.

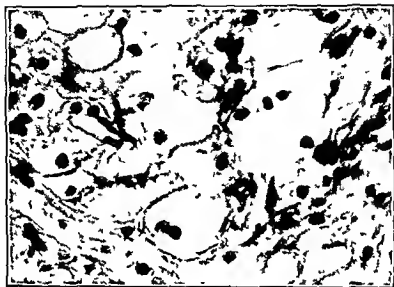


FIG. 43.—Xanthoma. The cells are round or polygonal, sharply outlined and have an abundant granular cytoplasm and small round nuclei. $\times 400$

Treatment is directed towards correcting the underlying systemic disturbance. The *prognosis* depends entirely upon the associated conditions which consist of severe liver damage, renal disease, cardiovascular disturbances, involvement of the pituitary and diabetes mellitus.

Melanoblastoma—This is a highly malignant neoplasm that usually arises in the skin and in the eye but sometimes originates in the brain and perhaps in the adrenal. In an attempt to indicate its histogenesis it has been called melanocarcinoma, melanoepithelioma, nevocarcinoma, melano-sarcoma and simply melanoma or malignant melanoma. The term melanoblastoma appears to be most suitable not only because it is a tumor of melanoblasts but also because, as has already been pointed out, melanoblasts arise from nerves and not from epithelial or mesodermal tissue. The neoplasm affects both sexes with equal frequency, is rarely found in negroes, and occurs at any age although two thirds of the patients are beyond the age of forty years. The lesions may be located in any portion of the skin, but they predominate in the lower extremities, face and upper limbs. The forerunner of cutaneous melanoblastoma is usually the slate blue or black, smooth, flat non-hairy pigmented nevus. The first indication of a malignant change is an increase in size, a deepening of the pigmentation, or the appearance of single or multiple peripheral nodules. Sometimes the nodules appear before there is any grossly demonstrable alteration in the nevus and, indeed, before there is even any histologic change to indicate a malignant trans-

formation. Repeated trauma and irritation are extremely important factors in converting a quiescent nevus into a melanoblastoma.

Clinically, the primary tumor may appear similar to its predecessor or it may be a large, polypoid, fungating and ulcerating mass that



FIG. 44.

FIG. 45.

FIG. 44.—Melanoblastoma There are numerous small, blue-black, intradermal, tumor nodules each of which resembles a blue-black nevus

FIG. 45 —Melanoblastoma The mass is large, black, fungating and superficially ulcerated.

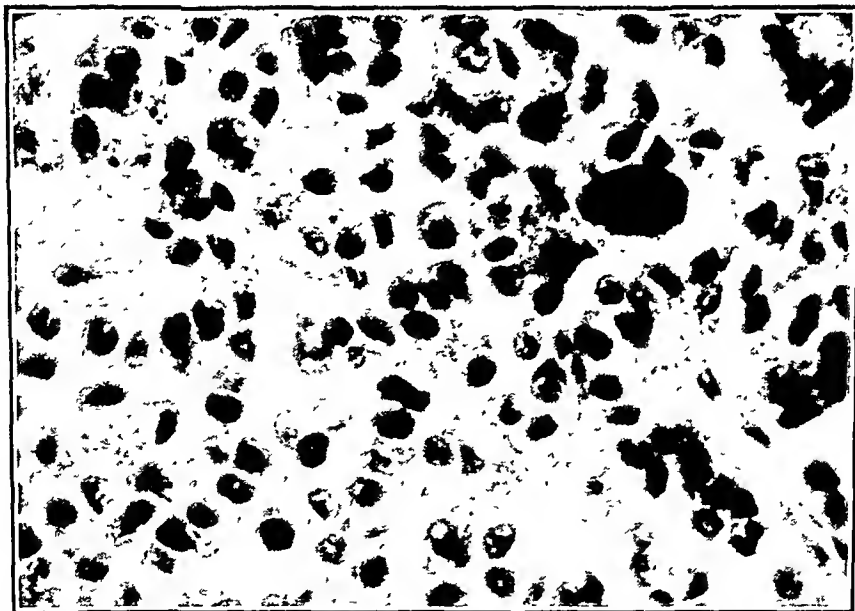


FIG. 46 —Melanoblastoma The cells vary considerably in shape and size Melanin is aggregated in a few large clumps x 400.

measures as much as 10 cm. in diameter (Figs. 44 and 45). It may be coal black in color or it may contain no pigment whatsoever. *Dissemination* of the tumor is by way of blood and lymph channels. By the time the patient is first examined the regional lymph nodes may be involved, there may be distant metastases in any of the organs, or there may be literally thousands of small nodules seeded

throughout the cutis and subcutis of the entire body. The amount of pigment in secondary tumors usually parallels that in the primary growth. The histologic structure of melanoblastoma is extremely variable (Fig 46). The cells are arranged singly, diffusely, in cords, sheets, or whorls. They are small or of giant proportions and are round, oval, spindle, polygonal or irregular. The cytoplasm may be scanty but usually it is quite abundant and deeply eosinophilic. The nuclei are single or multiple, round, oval, spindle, irregular, frequently bizarre and usually extremely hyperchromatic. Mitoses are, as a rule, not numerous. The supporting stroma is composed of scanty loose connective tissue or of dense fibrous tissue that almost completely replaces the tumor cells. Blood vessels may be numerous or scanty. In some tumors the cells are well preserved but in others there are large areas of necrosis, and the viable cells have a tendency to be grouped around engorged capillaries. The amount of melanin varies. Sometimes it is scanty and readily found only in dopa stained sections. At other times it is so abundant that it completely overshadows all underlying structures.

The diagnosis of melanoblastoma is easily established from the gross appearance of the lesion or lesions and is readily confirmed histologically. If the tumor is localized or if it has metastasized to the regional nodes then wide surgical excision with removal of the lymph nodes is indicated but blood borne metastasis precludes operation. Irradiation has little or no beneficial effect. The prognosis must always be guarded for patients who were apparently cured have been known to die of metastatic melanoblastoma as long as thirty years after the primary growth was removed.



Fig 47 — Neuroma. Several nerve bundles are surrounded by bundles of dense fibrous tissue. $\times 400$

Neuroma — A neuroma is a bulbous enlargement of an injured or severed nerve and not a true neoplasm. It is of frequent occurrence in amputations and is a common cause of the "painful stump."

After a nerve has been partially or completely divided the cells of the nerve sheaths proliferate in an irregular manner to produce a tangled mass of connective tissue. Concomittantly, the axis cylinders also proliferate and, following the deranged pathways produced by the nerve sheaths, they too produce intertwining, coiled masses of nerve bundles and single axis cylinders that become irregularly intermingled with the newly formed connective tissue (Fig. 47). Conversion of the latter into dense fibrous tissue with its resulting contraction produces pressure upon the nerve endings and pain.

Neurofibroma.—A neurofibroma is a benign tumor that arises from the coverings of nerves. Its *histogenesis* is still in doubt, although most authors consider it to be of mesodermal origin and to arise from the epineurium, the perineurium and the endoneurium. Some, however, still think that it arises from the sheath of Schwann which is composed of specialized nerve cells and that it is, therefore,



FIG 48 —Neurofibroma The nuclei are arranged in parallel rows—the so-called palisade formation x 75.

of ectodermal origin. Proponents of the latter theory call the tumor a neurinoma or a schwannoma. The lesion is frequently single but it may be multiple in which case the condition is known as *neurofibromatosis* or *von Recklinghausen's disease*. The onset of the latter is at any age from birth to twenty-five years. It affects males twice as often as females and has a familial distribution. The tumors originate along the course of the nerves in the cutis, subcutis or in the deeper tissues. They are small pinhead sized nodules that gradually increase to as much as 5 cm. or more in diameter. The latter are sessile or pedunculated, are covered with intact skin, are soft or moderately firm, and are frequently associated with brown pigmentation of the integument. The lesions occur anywhere on the body from the scalp to the soles, are irregularly or symmetrically distributed, and vary in number from a few to hundreds. *Histologically*, they consist of intertwining bundles of spindle cells containing regular, evenly stained, spindle or oblong nuclei (Fig. 48).

The tumors may be cellular in which case the cytoplasm is scanty and highly stained, or they may be relatively acellular revealing an abundant amount of deeply eosinophilic collagenous cytoplasm. In typical neoplasms the nuclei are arranged in parallel rows and assume the so-called palisade formation—a feature which distinguishes these tumors from simple fibromas.

The diagnosis is made from the gross appearance and distribution of the lesions, and is easily confirmed histologically. Single tumors are excised widely and completely otherwise they will recur. Multiple lesions are usually too numerous to be removed and are, therefore, left alone. The prognosis depends upon the involvement of internal tissues and viscera with similar tumors and, more seriously, upon the presence or absence of a sarcomatous change. The latter occurs in 12 per cent of cases.

Kaposi's Sarcoma—Multiple idiopathic hemorrhagic sarcoma of Kaposi, or perhaps better abbreviated as Kaposi's sarcoma, is a



FIG. 49.—Kaposi's sarcoma. Small hemorrhagic new lesions are seen about the periphery. The central portion is ulcerated, scurred and pigmented.

chronic, slowly progressive disease the pathogenesis and character of which have not been agreed upon. It has been reported on from all countries but is particularly common in Russia, Poland and Northern Italy. Its incidence is greatest beyond the age of fifty.

years, although no age is exempt and cases have been recorded in children. The cutaneous eruption usually starts in one extremity (more often the lower), but at some time during its course it becomes bilateral and symmetrical. The *lesions* appear as sharply defined papules, nodules or macules of bright or deep red color (Fig. 49). With age they become elevated and the color changes first to blue and later to brown or black. The eruptions progress over a period of years, may become stationary, and sometimes undergo spontaneous regression leaving faded, scaly or pigmented foci. Usually the covering epidermis remains intact, but as a result of trauma or secondary infection, it may become ulcerated. With extension of the lesions into the deeper portions of the cutis, and even the subcutis, the lymphatic channels become blocked resulting in stasis of lymph, swelling of the limb and thickening and induration of the skin. The disease *advances* by the appearance of new nodules at the periphery and ultimately, after a period of a few months to twenty-five years, by metastasis to regional lymph nodes and viscera. *Death* is due to intercurrent infection, to hemorrhage from secondary lesions in the intestinal mucosa, or to metastases in other organs.

Histologically, the initial lesions look like simple cavernous or capillary hemangiomas (Fig. 50). Gradually, the vascular spaces

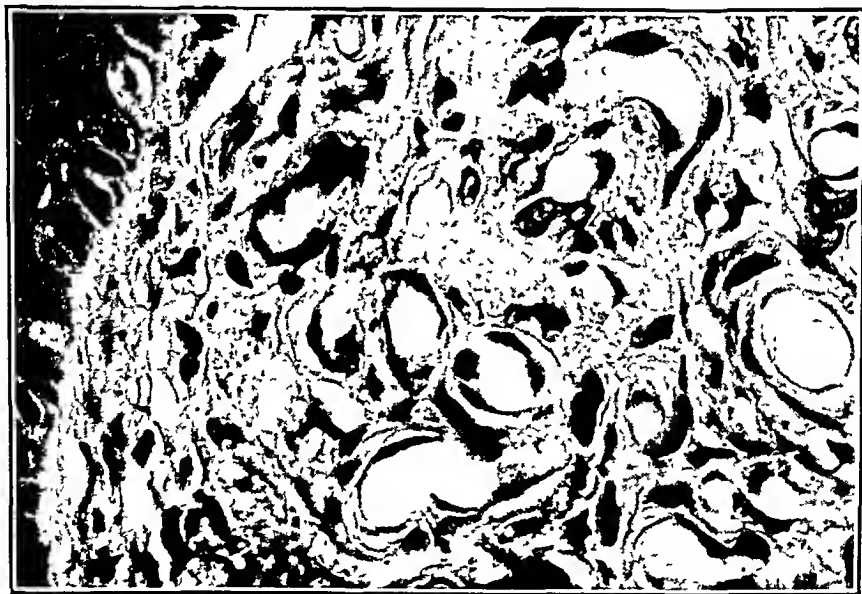


FIG. 50.—Kaposi sarcoma showing an early lesion composed entirely of capillaries and an acellular connective tissue stroma. $\times 200$.

become less definite. They lose their distinct endothelial lining and become imperceptibly blended with surrounding fusiform spindle cells that eventually replace most of the stroma. These cells have a scanty or moderate amount of cytoplasm, and relatively large plump, evenly but deeply stained nuclei. Their structure is indistinguishable from that of a fibrosarcoma. Concomitantly there are hemorrhages into the tissue with destruction of erythrocytes and liberation of iron containing pigment, and an infiltration with

lymphocytes, plasma cells and macrophages. Depending upon the age of the lesion and the amount of infection any one of the aforementioned processes may dominate the picture so that the lesion may resemble a hemangioma, a fibrosarcoma or a granuloma. For this reason much controversy has arisen not only as to whether the tumor is primarily of vascular or of fibroblastic origin, but indeed as to whether the lesion is a tumor at all. The behavior of the disease, however, with always a fatal termination, indicates that it is a malignant neoplasm, albeit of low grade, and the inevitable presence of blood vessels, both cavernous and capillary, makes the vascular component of paramount importance. It seems, therefore, that the lesion is a sarcoma of vessels and that its most appropriate designation is "angiosarcoma."

The diagnosis is made from the appearance and location of the tumors, the chronic course, and histologic examination of removed tissue. Treatment is most unsatisfactory. Irradiation will eradicate the lesions but when they return, as they always do, they become more resistant to subsequent roentgen therapy. Surgical excision is followed by new eruptions about the periphery and amputation of a limb will not preclude the development of nodules in the opposite extremity or metastatic foci in distant organs. The ultimate prognosis, therefore, is grave.

Glomal Tumor—This is a benign growth that arises in a glomus. A glomus is a normal subcutaneous arteriovenous anastomosis that



FIG. 51.—Glomus tumor illustrating a fibrous true capsule enclosing a mass of thin-walled blood channels. $\times 200$

regulates the peripheral circulation of blood and thus controls local and general temperature. It is composed of an afferent arteriole, a coiled and twisted anastomotic vessel, a primary collecting vein, a stroma of reticulum, nerves and muscle, and a capsule of connective tissue. Tumors of this apparatus are widely distributed over the body but are most common on the extremities and are particularly

frequent in the pulp of the fingers and in the nail bed. They are found only in adults and affect women more often than men. *Clinically*, they appear as round or oval, smooth, rose or purple, movable, exquisitely painful and tender nodules that measure as much as 12 mm. in diameter. *Histologically*, they consist of an overdevelopment of a normal glomus (Fig. 51). About the periphery there is a capsule of collagenous connective tissue. Into this enters a large nutrient arteriole that is surrounded by a network of non-medullated nerves. The central portion is composed of anastomosing thin walled blood channels that are very similar to those of a capillary or cavernous hemangioma. The stroma consists of loose or hyalinized connective tissue, cords or masses of elongated or polyhedral epithelioid and muscle cells that often undergo mucoid degeneration, elastic tissue, and nerve fibers. Because of this admixture the tumor is also known as an angioneuromyoma. The size and location of the nodule with a history of exquisite pain upon slightest provocation readily establishes a clinical diagnosis. *Treatment* consists of local excision.

Mixed tumors of the skin are composed of two or more types of tissue and are characterized by their pleomorphism. They are found in adults and are *located* not only near fissures, such as the lips, mouth, palate and lacrimal glands but also in the scalp, face, extremities and less commonly the trunk. They grow slowly over a period of many years and appear as single or multiple, firm or hard, freely movable, intradermal nodules that rarely grow larger than 3 cm. in diameter. Microscopically, they are surrounded by a connective tissue capsule in which there are often portions of sweat glands. The tumor proper is composed of both *ectodermal* and *mesodermal* elements. The former consists of recognizable remnants of sweat and sebaceous glands, nests of prickle cells, cysts lined with epithelium, or columns and islands of irregularly arranged epithelial cells. The *mesodermal* elements consist of loose, collagenous or myxomatous connective tissue, cartilage and lymphoid tissue. Although these tumors have been considered as true teratomata, they are probably nothing more than primary epithelial growths of the epidermis or its appendages that stimulate the mesoderm to metaplasia. *Treatment* consists of local excision. Recurrences are due to incomplete removal and rarely to a malignant transformation.

Secondary neoplasms of the skin are not common. They arise (1) as a direct extension from an adjacent tumor, (2) by way of the lymphatic vessels either as direct permeation or as emboli, and (3) by blood stream metastases from local or distant foci. In the integument the secondary deposits may be found in the subcutaneous tissue, in the dermis and, less commonly, in the epidermis. They appear as single or multiple sharply circumscribed nodules or diffusely infiltrating plaques that measure less than a millimeter to many centimeters in diameter. They are often located directly opposite or in the vicinity of the primary tumor, but sometimes they are irregularly distributed in distant areas. They occur singly or in crops and grow both by increasing in size and by forming second-

ary satellite nodules about their periphery. Although most malignant tumors have been known to metastasize to the skin the most common offenders are melanoblastoma, and carcinoma of the breast, gastrointestinal tract, ovary, kidney and lung. Usually the cutaneous lesions appear late in the disease but sometimes they become manifest months before the primary tumor is discovered. As a rule secondary cancer of the skin is only of academic interest and the prognosis is hopeless.

Leukemids are leukocytic infiltrations of the skin accompanying myelogenous, lymphocytic and monocytic leukemia. *Clinically*, the eruptions occur anywhere on the body as scattered or numerous, sharply circumscribed, firm, brown, blue, purple or red, elevated or buried nodules or plaques that measure as much as 2 cm. in diameter. Usually the epidermis is intact but sometimes it becomes scaly, crusts and ulcerates. The underlying nodule then becomes soft, necrotic, discharges pus, and heals. Some of the nodules regress spontaneously. *Microscopically*, the infiltrations originate around hair shaft and sebaceous and sweat glands from where they spread to involve the entire thickness of the dermis and adjacent subcutaneous tissue. In myelogenous leukemia the infiltrates consist principally of myeloid cells, in lymphocytic leukemia of lymphoid cells and in monocytic leukemia of monocytic cells. Seldom is it necessary to resort to histologic examination of a cutaneous nodule for the diagnosis can be readily established from a smear of the peripheral blood. *Treatment* is directed toward the primary disease. The prognosis is poor.

Hodgkin's Disease and Mycosis Fungoides—The status of mycosis fungoides as a separate disease has been questioned since it was originally described in 1812. There are those who consider it a specific cutaneous disorder and those who regard it as a cutaneous manifestation of any one of the lymphoblastoma group of diseases. Certainly, the location and gross appearance of the eruptions in mycosis fungoides can not be distinguished from those in Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma and the leukemids. *Histologically*, each one of these with the exception of Hodgkin's disease can be readily segregated. In both Hodgkin's disease and mycosis fungoides, however, the infiltrating cells consist of neutrophils, eosinophiles, plasma cells, lymphocytes, epithelioid cells and giant cells of the Sternberg-Reed type. Because of this similarity the question arises 'are Hodgkin's disease and mycosis fungoides one and the same condition?' Those authors who consider them as separate entities maintain (1) that mycosis fungoides always involves the skin and uncommonly affects the lymph nodes and internal organs whereas the reverse is true of Hodgkin's disease, (2) that the lesions in the former disappear by absorption and those in the latter by excision and necrosis and (3) that the infiltrations in mycosis fungoides are located in the upper third of the dermis whereas those in Hodgkin's disease are found in the middle and lower thirds. From a study of our material and a review of the literature my own opinion is that the line of demarcation is somewhat indistinct to say the least and that mycosis fungoides is

nothing more than Hodgkin's disease with specific lesions appearing first in the skin.

Mechanical Disturbances.—Tattoo.—A tattoo is an artificially produced permanent pigmentation of the skin. The motives underlying tattooing are variable. Among primitive people it has a religious background, and is used for identification to ward off disease and to terrify the enemy in battle. Among civilized people it is performed most often from curiosity and for sexual reasons. Modern tattooers drive the pigment into the dermis with an electric needle. A black or blue color is imparted by india ink, a red color by mercuric sulfide and a yellow color by kurkuma. The skin becomes swollen, hot and crusted. In a week the crust falls off, the holes are re-epithelialized and the design becomes clear. *Histologically*, the dermis in the black and blue areas shows particles of pigment between connective tissue cells, but in the red areas the epidermis may show hyperkeratosis and acanthosis, and about the particles there may be an infiltration with lymphocytes eosinophiles and fibroblasts. The incidence of syphilis among tattooed persons is less than it is among the general population of the same stratum.

Keloid.—Keloids are benign proliferations of fibrous connective tissue in the dermis. They always arise as a result of trauma, the

severity of which ranges from that of an insect bite to that of an extensive burn. They are found most often between the ages of ten and twenty years, tend to regress or disappear spontaneously after the menopause, are more frequent in negroes than in white people, have a familial tendency, and are not related to syphilis or tuberculosis. They may be single or multiple and have a predilection for the sternum, back and ears. They appear as firm, raised, smooth, shiny, sometimes tender, round, oval linear, lobulated or



FIG 52 —Keloid involving an ear

otherwise bizarre nodules that range in color from pink to red, white or brown, and in size from a few millimeters to many centimeters (Fig. 52). *Microscopically*, the early keloid consists of irregularly arranged bundles of loose, or compact, relatively cellular fibrous connective tissue throughout which there are scattered a few engorged capillaries. About the periphery the vessels are more prominent and the overlying epithelium is acanthotic. With age the fibrous tissue becomes more compact, less cellular and more collagenous. The capillaries disappear, the epidermis becomes attenuated and the rete cones vanish. The *diagnosis* is made from the characteristic gross appearance of the growths often coupled with a history of trauma. Virtually every conceivable method of *treatment* has been tried. The most efficacious appears to be roentgen therapy, or surgical excision followed by irradiation which is

started preferably on the day after the operation. Recurrences are frequent, but a sarcomatous change is rare.

Gangrene—Gangrene is death of tissue and, although actually synonymous with necrosis, it is generally used to connote a massive destruction. It can occur anywhere in the body both internally and externally. The latter is usually found in the distal portions of the extremities. Generally, the primary cause is interference with the blood supply to an area, although on some occasions it is the result of bacterial infection alone. Conventionally, peripheral gangrene is divided into a *dry* and a *moist* type. The former comes about



FIG. 53—Dry gangrene about the medial malleolus and moist gangrene with ectodermal blebs involving the rest of the foot.

slowly and is dependent upon a gradual diminution in flow of arterial blood in the presence of an adequate venous drainage. The result is an ischemic necrosis. *Moist gangrene* develops more rapidly and is dependent upon not only an inadequate supply of arterial blood but also upon an inadequate venous drainage. The result is an enlarged, boggy limb or portion of a limb. Bacteria, particularly micro-aerophilic streptococcus and *Clostridium welchii*, are present in each. The media for their growth is poor in dry gangrene, but it is excellent in moist gangrene under which circumstances they multiply profusely. As a result of their luxuriant growth more tissue is destroyed, both by the action of the organisms and indirectly from further interruption of arterial blood supply. It is because of this vicious cycle that moist gangrene tends to spread much more rapidly than does the dry type. Frequently, bacterial multiplication, and specifically that of *Clostridium welchii*, is accompanied by the formation of gas bubbles within the tissues and the lesion is then called *gas gangrene*.

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severity of which ranges from that of an insect bite to that of an extensive burn. They are found most often between the ages of ten and twenty years, tend to regress or disappear spontaneously after the menopause, are more frequent in negroes than in white people, have a familial tendency, and are not related to syphilis or tuberculosis. They may be single or multiple and have a predilection for the sternum, back and ears. They *appear as* firm, raised, smooth, shiny, sometimes tender, round, oval linear, lobulated or



FIG 52 —Keloid involving an ear.

otherwise bizarre nodules that range in color from pink to red, white or brown, and in size from a few millimeters to many centimeters (Fig. 52). *Microscopically*, the early keloid consists of irregularly arranged bundles of loose, or compact, relatively cellular fibrous connective tissue throughout which there are scattered a few engorged capillaries. About the periphery the vessels are more prominent and the overlying epithelium is acanthotic. With age the fibrous tissue becomes more compact, less cellular and more collagenous. The capillaries disappear, the epidermis becomes attenuated and the rete cones vanish. The *diagnosis* is made from the characteristic gross appearance of the growths often coupled with a history of trauma. Virtually every conceivable method of *treatment* has been tried. The most efficacious appears to be roentgen therapy, or surgical excision followed by irradiation which is

arteries and is usually found beyond the age of fifty years but when it is associated with diabetes mellitus it occurs a decade earlier. Of the numerous theories advanced to explain the cause only two need be mentioned, (1) that it is a manifestation of a wear and tear phenomenon resulting from continued trauma on the vessel wall by the ever present expanding column of blood and, (2) that it is the result of deranged cholesterol and lipid metabolism. Pathologically, the earliest lesions appear as raised, yellow, intimal thickenings which histologically consist of a mixture of proliferated connective tissue cells and phagocytes loaded with fat. With progression and further degeneration the plaques become soft, mushy, and ultimately break through the intima to produce an ulcer. The roughened surface predisposes to thrombosis which eventuates in partial or complete occlusion of the lumen (Fig 54). Simultaneously, the media becomes thinned, calcified or ossified, replaced with fibrous tissue and infiltrated with lymphocytes. The adventitia discloses irregular areas of fibrosis.

Thrombo-angitis obliterans or Buerger's disease is a slowly progressive, inflammatory disease of the peripheral arteries, veins and nerves. It occurs almost entirely in men between the ages of twenty-five and forty years, is accompanied by intermittent pain in the involved limb, results in obliteration of the vascular lumens, and eventuates in necrosis and gangrene of the digit or extremity. It affects the lower member more often than the upper and characteristically starts in the tibial, radial and ulnar arteries. Although numerous diversified agents such as the male sex hormone, tobacco, viruses and bacteria have been considered as possible causes of the

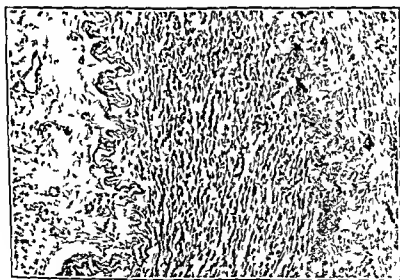


Fig 55—Thrombo-angitis obliterans illustrating a recanalized thrombus in the lumen and fibrosis of the media and adventitia. $\times 75$

disease its etiology still remains an enigma. Pathologic changes as seen in specimens ordinarily sent to the laboratory consist of a matting together of the medium sized arteries, veins and accom-

Since gangrene results from an inadequate supply of arterial blood, the *part first affected* is usually that which is furthest from the heart, namely, the tips of the digits. An area of focal necrosis often appears lateral to the nail bed whence it spreads to involve the entire digit, foot or hand, and then leg or arm. Rarely does it extend above the knee or the elbow. In dry gangrene the part becomes shrivelled, shrunken, parchment-like, and mummified (Fig. 53). As a result of liberation of blood pigments the color changes vary from greenish yellow to deep brown and black. The advancing edge of the necrotic area is usually sharp and, in the adjacent normal tissue, there is a low grade inflammatory reaction. In moist gangrene the part is swollen, multicolored, not sharply delineated and, as a result of gas formation, it is often crepitant. Absorption of toxic products of bacterial and tissue origin results in severe constitutional disturbances. *Treatment* of gangrene varies somewhat according to the cause, but in general it consists of avoiding injury such as rubbing of shoes, callous formation, application of irritating drugs and so forth. Unfortunately, in most cases, amputation of a digit or extremity ultimately becomes necessary.

Some of the specific *causes* of peripheral gangrene are arteriosclerosis obliterans, thrombo-angiitis obliterans, Monckeberg's sclerosis with secondary atheromatous changes, traumatic disruption of the vessels, thrombosis, embolism, arteriovenous fistula, thrombophlebitis and spasm of arteries such as seen in trench or immersion foot, frost bite, Raynaud's disease, livedo reticularis, and ergotism. Some of these are self explanatory, some are too rare to merit further elucidation, but a word or two about the others is almost mandatory

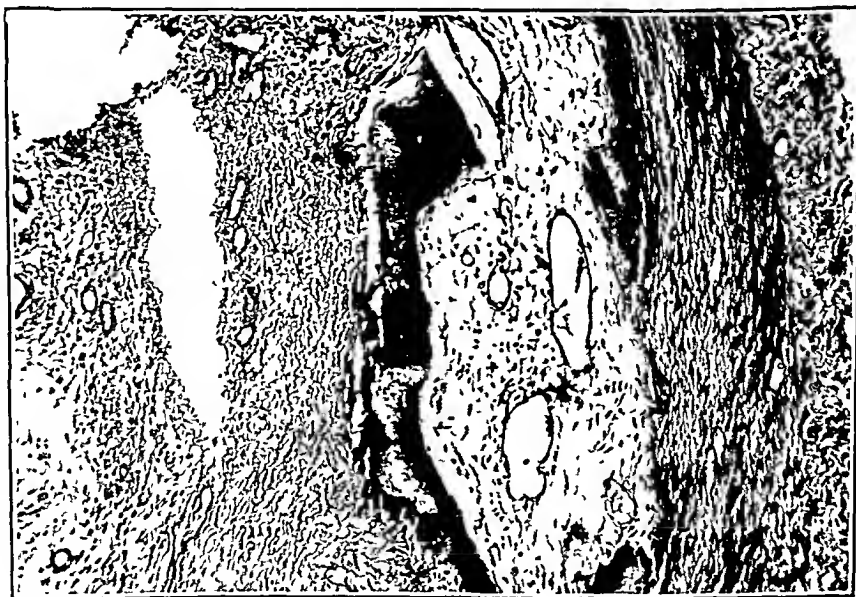


FIG. 54.—Arteriosclerosis obliterans showing from left to right an organized thrombus in the lumen, fibrous thickening of the intima, and ossification of the media ' x 75.

Arteriosclerosis obliterans may be defined as arteriosclerosis in which the arterial lumen becomes gradually and progressively occluded. It is the most common cause of occlusion of the peripheral

fifteen per cent of the population, are found most often between the ages of thirty and fifty years, and affect two women to every man. In some cases they result from an obvious obstruction such as thrombosis, thrombophlebitis and pressure upon the iliac veins and inferior vena cava by a pregnant uterus, ascites or abdominal tumors. In other cases there are no obvious causes and they are then considered to arise on the basis of a hereditary weakness in the walls of the veins, and valves. Our own studies revealed a deficiency of elastic fibers and a thinning or complete absence of the muscle coat of the wall of the sinus of the sapheno-femoral valve in eighty-four per cent of an unselected group of 100 cadavers. It seems plausible, therefore, that this is a potential congenital weak spot which upon dilatation is followed by valvular insufficiency and stretching of the saphenous vein and its tributaries.

Symptoms may be entirely lacking or may consist of muscle fatigue, cramps, pain, burning and itching. *Grossly*, the veins become dilated, elongated, tortuous, and knotty (Fig 56). The walls become thickened or thinned, the valves atrophy and disappear, and the lumen sometimes becomes occluded with a thrombus. *Histologically*, the muscle coat in veins with thick walls is hypertrophied but in those with thin walls it is atrophied and replaced with fibrous tissue. The intima is thickened and fibrotic and the lumen may contain a recent or an organized and recanalized thrombus. The *complications* of varicose veins are eczematoid dermatitis, ulceration with brown pigmentation of the skin, hemorrhage and thrombophlebitis. *Treatment* consists of prevention, intravascular injection of sclerosing fluids, and ligation of the saphenous vein at its entrance into the femoral vein. The *end results* are generally quite satisfactory.



FIG 56—Varicose veins. The veins are nodular and tortuous and the skin over the lower portion of the leg is fibrotic pigmented and ulcerated.

panying nerves by fibrous tissue. Cross section through the mass discloses the coats of the artery and sometimes the veins to be well preserved and the vascular lumens to be filled with a red, grey, white or yellow thrombus. There is no calcification. *Histologically*, the lumens of the artery and the veins are partly or completely filled with recent or organized and recanalized thrombi (Fig. 55). There is extensive endothelial proliferation and lymphocytic infiltration of the intima. The veins in addition may show, along the margin of the thrombi, giant cells of the foreign body type. The muscle coats, other than disclosing some increase in fibrous tissue and capillaries, are remarkably well preserved. The adventitia and surrounding tissue show extensive fibrosis and some perivascular cuffing of lymphocytes.

Mönckeberg's sclerosis is a disease of the larger arteries of the extremities characterized by calcification of the medial coat. It is of little clinical significance unless it is associated with arteriosclerosis obliterans. In such cases the symptoms are referable to the latter disease.

Spasm of arteries may occur under various conditions. *Trench foot* results from prolonged exposure to cold atmosphere and *immersion foot* from similar exposure to cold water. Both occur among troops in warfare and differ from *frost bite* in that the temperature is above freezing point. The mechanism of producing gangrene in these conditions is somewhat similar to that in *ergotism*. Prolonged spasm of arterioles results in injury to the endothelium, dilatation of the capillary bed distal to the spasm and the formation of agglutinative thrombi in the arteries, capillaries and veins. Secondary fibrosis of the vessel walls and surrounding inflammatory reaction are common. *Raynaud's disease* is a spastic phenomenon of the arterioles of particularly the upper extremities. The disease is found much more frequently in females than in males, usually begins in the second decade, is bilateral and symmetrical, and is most often confined to the distal portions of the limbs. Upon exposure to cold a series of characteristic color changes, consisting of pallor, cyanosis and redness, develop first in the fingers and later in the hands. In advanced stages, foci of necrosis may appear at the tips of the fingers but extensive gangrene is usually not encountered. Lack of opportunity to examine pathologic material leaves the histologic changes in the realm of speculation. *Livedo reticularis* is likewise primarily a vasospastic disease of the extremities that is manifest by a mottled, reddish blue discoloration of the skin. Its onset is usually in the third or fourth decades of life. Occasionally there is an accompanying coldness, tingling and aching of the lower extremities and in a few cases focal necrosis and gangrene have been described. Sometimes there are no demonstrable pathologic changes in the vessels but at other times there is a proliferation of the intima of the arteries, arterioles and veins, and a perivascular fibrosis and leukocytic infiltration.

Varicose Veins.—Varicose veins are dilated veins. Without further specification the term ordinarily implies dilatation of the long saphenous veins and their tributaries. They occur in about

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Chapter II

BREAST

EMBRYOLOGY

THE first indication of mammary glands in man occurs in the sixth week of embryonic life as a bilateral linear thickening of the ectoderm that extends from the base of the upper limb to the inguinal fold. Elevation of the line by the third month forms a distinct ridge known as the mammary ridge which, however, is conspicuous only in its cephalic portion. Elsewhere, it disappears early. At the site of the future breast the epidermal thickening increases in size to form first a globular, and then a lobulated mass of epithelium. By the fifth month the latter forms from fifteen to twenty-five solid cords of tissue which are the future mammary ducts and the distal portions of these arborize to form secretory acini. At approximately the seventh month of intrauterine life lumens appear within the acini and ducts, and the overlying ectoderm becomes excavated. At birth the entire mass becomes elevated to form the nipple and is surrounded by a circular area of discoloration known as the areolar. In males the breasts remain in this rudimentary stage throughout life. In females, however, at the age of puberty they undergo a substantial increase in size as a result of hypertrophy, hyperplasia and accumulation of fat.

ANATOMY

Although the shape and size of the adult, resting, female breast varies, generally speaking it is more or less a conical hemisphere that extends from the second rib superiorly to the sixth rib inferiorly and from the lateral border of the sternum medially to the midaxillary line laterally. The nipple is at the level of the fourth intercostal space. Beneath the skin a fascial investment sends fibrous tissue septa deep into the mammary tissue that divide the gland into from fifteen to twenty-five lobules. Each lobule contains fat and fibrous tissue that surround the alveoli, alveolar ducts and excretory ducts and is thus a complete unit in itself. The arteries to the breast arise from the internal mammary, the thoracic branches of the axillary and the intercostal arteries, and the veins empty into the axillary and internal mammary veins. The nerves to the breast arise from the fourth, fifth and sixth thoracic nerves. The lymphatic vessels start on the walls of the ducts and form two plexuses—one situated beneath the areola and the other in the fascia on the pectoralis major muscle. The former drains the central part of the breast, the nipple, the areola and the immediately surrounding skin and communicates with the deeper plexus. Efferent vessels from the latter empty into the axillary, subclavicular, internal mammary and extraperitoneal lymph nodes and each of these drains the

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contains modified sweat glands that are called the *glands of Montgomery*. The nipple contains the openings of the *excretory ducts* which are lined with modified squamous epithelium and are covered with a layer of longitudinal smooth muscle. The *alveolar ducts* and *alveoli* are composed from without in of a basement membrane, myoepithelial cells and a single row of low columnar cells (Fig 57). Both the alveoli and alveolar ducts are surrounded by loose, cellular, somewhat edematous connective tissue which disappears as the alveoli proliferate and reappears as they involute (Fig 58). Between the lobules the connective tissue is dense and collagenous.

The breast is not a static organ but is subject to hormonal influences. In the *postovulatory phase* of the menstrual cycle it becomes full, somewhat turgid and often painful. This is due to congestion and edema of the interstitial connective tissue and to a hyperplasia of acini. During the first half of *pregnancy* there is a rapid proliferation of the epithelium at the ends of the excretory ducts, with formation of new alveolar ducts and acini. During the second half of gestation the newly formed cells gradually acquire droplets of secretion which at the end of pregnancy are extruded as colostrum and during lactation as milk (Fig 59). With the end of nursing the secretion in the acini is absorbed, the formation of new milk ceases and the gland gradually returns to a resting stage. *Atrophy* and disappearance of the glandular elements occur in old age and the gland tends to return to its prepubertal stage.

PATHOLOGY

Congenital Anomalies—Congenital abnormalities of the breast are not particularly common. Lesions of the nipple consist of a failure of elevation resulting in an *inversion*, a decrease in size (*microthelia*), and absence (*athelia*), and an excess number (*polythelia*) which may occur anywhere along the embryonic mammary ridge. These anomalies may be unilateral or bilateral and may occur independently or in association with the following abnormalities in the breast, absence (*amastia*) decrease in size (*micro-mastia*) and an excess number (*polymastia*). Although the latter can occur at any point along a line from the base of the upper extremity to the groin *aberrant mammary tissue* is frequently encountered in the axilla and only rarely in other areas. In the axilla it is of surgical significance firstly, because it may produce a painful swelling not only during pregnancy and lactation but also during the postovulatory phase of the menstrual cycle, secondly because it predisposes to inflammation and abscess formation, and thirdly because it may be a site for primary carcinoma. *Hypertrophy* of the female breast may be unilateral or more often bilateral, usually occurs after puberty but may be present during childhood, and consists of a hyperplasia of glandular elements, connective tissue and fat tissue.

Gynecomastia—Gynecomastia may be defined as an enlargement of the male breast that is not due to an accumulation of fat or to the presence of true tumors. It is unilateral more often than bilateral,

lateral, the upper, the medial and the infero-medial portions of the breast respectively.

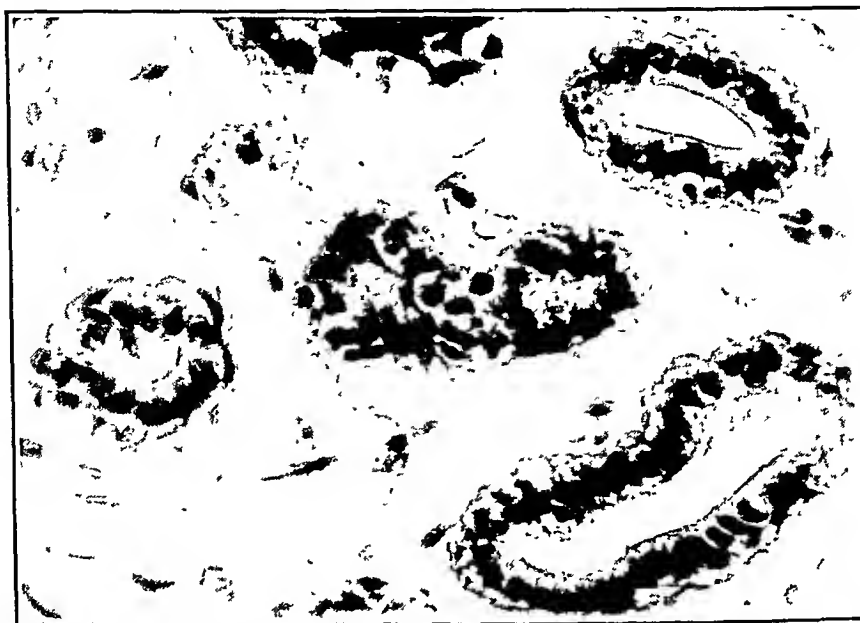


FIG 57—Normal alveoli showing from without in a basement membrane, scattered elongated myo-epithelial cells and a single row of low columnar cells. x 400.

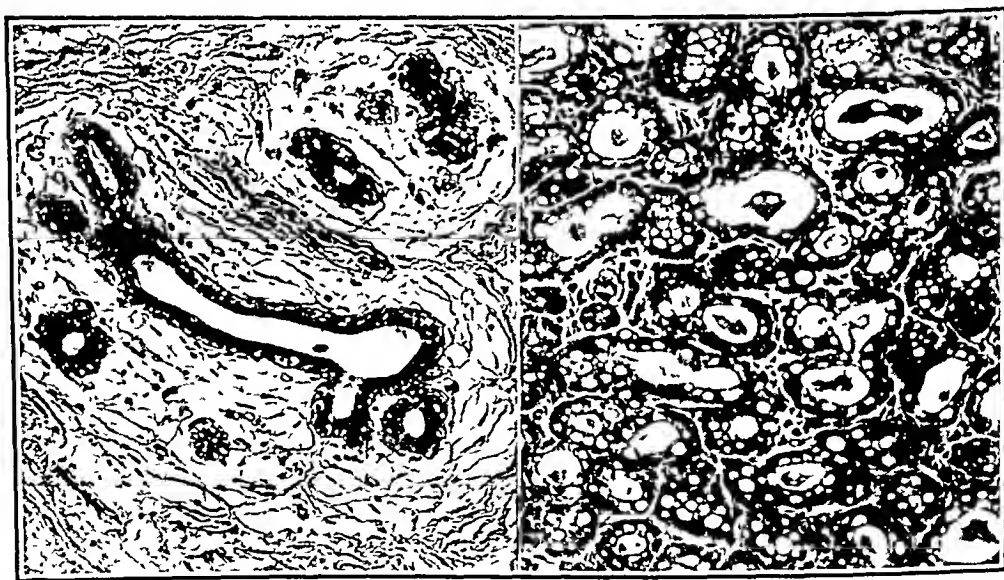


FIG 58

FIG. 59.

FIG. 58 —Normal mammary lobule showing an alveolar duct budding into alveoli. The immediately adjacent tissue is loose and myxomatous whereas the peripheral tissue is dense and collagenous x 100

FIG. 59.—Physiologic hyperplasia of the breast illustrating numerous alveoli lined with a single layer of secreting cuboidal cells. The lumens contain precipitated secretion. x 200.

Histologically, the skin covering the mammary gland is the same as that covering other portions of the body. Along the margin of the areola there are sweat and hairless sebaceous glands that empty onto the surface by a common opening. More centrally the areola

cillin therapy. When the lesion suppurates, however, it must be drained surgically.



FIG. 60—Acute mastitis showing three small abscesses

Chronic Specific Inflammation—As compared with other lesions of the mammary gland chronic specific infections are not common. Primary and secondary *sypphilis* may affect the nipple, areola and skin and, rarely, tertiary lesions may be found within the parenchyma proper. *Actinomycosis* of the breast is also extremely rare and in most instances the infection enters the organ not from the outside but as an extension through the chest wall from a pulmonary lesion. Tuberculosis and plasma cell mastitis while still uncommon are more frequent than the aforementioned diseases and will, therefore, be considered in more detail.

Tuberculosis—Tuberculosis of the mammary gland occurs in from 0.54 to 1.87 per cent of all lesions of the breast. It affects twenty women to every man, is found between the ages of twenty to fifty years, and is more frequent in married women who have borne children. The causative organism is the tubercle bacillus, usually of the bovine strain, that gains entrance by way of the ducts, abrasions of the nipple and skin, the blood stream, the lymphatic vessels and direct extension from neighboring tissues. Trauma is cited as a predisposing cause in 7 per cent of cases. In three-quarters of the cases, the first symptom is a painless lump in the breast. Pain occurs as the initial symptom in only 8 per cent of cases. Patients may also complain of purulent discharge from the nipple, draining cutaneous sinuses over other areas of the breast

has no predilection for any single race, is found at any age but is more frequent in the third decade of life, and does not regress spontaneously. The duration is from a few months to many years and the symptoms consist of enlargement, pain and tenderness. In some cases the *cause* can be attributed to an increase in estrogens but in others hormonal disturbances are not demonstrable. Although trauma and irritation are often incriminated as causative agents it is probable that they merely served to draw attention to the enlargement and are not the initiating factors in its development. The nipple and areola are usually normal but occasionally the former may enlarge and project above the surface, and the latter may widen and show an increase in pigmentation. The *breast* is smooth in outline, weighs as much as 600 gm. and discloses a firm, moist, homogeneously pale grey, not encapsulated but clearly defined mass of tissue. *Histologically*, there is a proliferation of the interlobular and intralobular connective tissue, an elongation and branching of the ducts without the formation of acini, and a periductal or diffuse infiltration with plasma cells, lymphocytes and, less often, neutrophils and eosinophiles. *Treatment* is surgical excision and is indicated when there is anxiety, mortification, pain or a suspicion of a cancerous transformation. The latter, however, if it occurs at all, is extremely rare.

Inflammation.—Acute Inflammation.—Acute inflammation of the mammary gland is called *acute mastitis*. Although it may affect either sex and occur at any age it is most often found in women within the first three weeks of the puerperium. The predisposing *causes* are trauma, cracked or fissured nipples, vascular engorgement and stasis of milk. The immediate cause is a pyogenic organism, which in most instances is staphylococcus aureus, and the route of invasion is ascension along the ducts, permeation along lymphatic channels, metastasis by way of the blood stream from a distant focus, or by direct extension from neighboring structures. The *symptoms* consist of a sudden onset of pain in the breast, chills, and fever which may reach as high as 106° F. The *breast* is enlarged, tense, exquisitely tender, erythematous and contains within its substance an indurated mass. In three or four days the induration gives way to liquifaction and abscess formation which may or may not be readily detected clinically. The area of suppuration may be small or large, single or multiple and may be located beneath the areola, beneath the skin, within the breast, beneath the breast or beneath the pectoral muscle (Fig. 60). In the early stages there is no sharp line of demarcation between normal tissue, abscess wall and the central area of liquifaction or pus, but within a few days these zones become clearly delineated. Initially, the *histologic* changes are those of an acute cellulitis and later, when suppuration supervenes, they are those of an acute or chronic abscess. The diagnosis is sometimes difficult for at first the lesion closely simulates an inflammatory carcinoma, and an old, contracted abscess may not be distinguishable from a scirrhus carcinoma. In the early stages *treatment* consists of care of cracks and fissures, prevention of trauma, emptying of all secretions, diathermy, irradiation or peni-

cillin therapy. When the lesion suppurates, however, it must be drained surgically.



FIG. 60—Acute mastitis showing three small abscesses.

Chronic Specific Inflammation—As compared with other lesions of the mammary gland chronic specific infections are not common. Primary and secondary *syphilis* may affect the nipple, areola and skin and, rarely, tertiary lesions may be found within the parenchyma proper. *Actinomyces* of the breast is also extremely rare and in most instances the infection enters the organ not from the outside but as an extension through the chest wall from a pulmonary lesion. Tuberculosis and plasma cell mastitis while still uncommon are more frequent than the aforementioned diseases and will, therefore, be considered in more detail.

Tuberculosis—Tuberculosis of the mammary gland occurs in from 0.54 to 1.87 per cent of all lesions of the breast. It affects twenty women to every man, is found between the ages of twenty to fifty years, and is more frequent in married women who have borne children. The causative organism is the tubercle bacillus, usually of the bovine strain that gains entrance by way of the ducts, abrasions of the nipple and skin, the blood stream, the lymphatic vessels and direct extension from neighboring tissues. Trauma is cited as a predisposing cause in 7 per cent of cases. In three-quarters of the cases, the first symptom is a painless lump in the breast. Pain occurs as the initial symptom in only 8 per cent of cases. Patients may also complain of purulent discharge from the nipple, draining cutaneous sinuses over other areas of the breast.

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cells the supporting tissue contains giant cells, foam cells and fatty acid crystals. Sections of lymph nodes show a hyperplasia of the follicles and a mild leukocytic infiltration. The cause of the disease is not known but the lesion is thought to result from the chemical effect of decomposed fatty material. The only means of differentiating plasma cell mastitis from carcinoma clinically is to elicit a history of erythema, pain, discomfort, and tenderness that precedes the formation of a residual tumor by several weeks or months. Treatment consists of local excision. The prognosis is excellent. None of the patients has as yet been known to develop carcinoma.

Tumors—Since the skin covering the breasts is the same as that covering other portions of the body it is not surprising that any one of the cutaneous lesions, which have been described in the preceding chapter, may also be encountered in the integument of the mammary glands. Of particular interest, perhaps, are diseases of the nipple

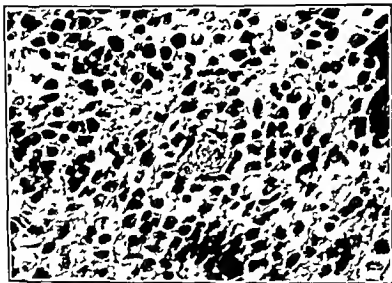


FIG. 61.—Plasma cell mastitis disclosing a diffuse infiltration with plasma cells. $\times 400$

which, among others include Paget's disease, epidermal papilloma, squamous and basal cell carcinoma, and cysts of sebaceous and sweat glands. In addition to the integument, however, the breast is composed of a variety of tissues of both ectodermal and mesodermal origin and each is capable of giving rise to an innocent or a malignant tumor. Thus from epithelium there develops a duct papilloma, a cystic hyperplasia and a carcinoma; from connective tissue a fibroma and a fibrosarcoma; from epithelial and connective tissue a fibroadenoma and an adenofibrosarcoma; from fat a lipoma and a liposarcoma; from muscle a leiomyoma and a leiomyosarcoma; from nerves a neuroma, a neurofibroma and a neurofibrosarcoma; from vessels a lymphangioma, a hemangioma and a hemangiosarcoma; from lymphoid tissue a lymphosarcoma or Hodgkin's disease, and from mesodermal elements as a result of metaplasia a giant cell tumor, a chondroma, a chondrosarcoma, an osteoma and an osteo-

and enlarged axillary nodes. Physical examination discloses the disease to be unilateral in about 97 per cent of cases. The skin may be normal, flat, red, puckered or contain a draining sinus tract. The underlying mass is usually single, firm, solid or cystic, not freely movable and measures several centimeters in diameter. The axillary and supraclavicular lymph nodes are enlarged in 50 per cent of the cases in which the disease is primary in the breast, that is, in patients who have no demonstrable tuberculous lesions elsewhere in the body, and in 100 per cent of the cases in which the mammary lesion is secondary to other foci.

Grossly, the lesion is sharply delineated but not encapsulated, measures a few or several centimeters in diameter and is firm, solid and grayish white or more often cystic. The wall of the latter is firm, thick, grey and fibrous; the lining is composed of yellowish gray friable necrotic tissue, and the lumen is filled with thick, light green pus or caseous material. *Histologically*, there are numerous or scanty tubercles similar to those already described in the chapter on the skin.

Clinically, tuberculosis of the mammary gland is frequently confused with carcinoma and less often with plasma cell mastitis, fat necrosis and, in the presence of sinuses, with actinomycosis. Examination of purulent discharge from the nipple or from a ruptured lesion for tubercle bacilli will, however, often settle the diagnosis. The *treatment* of choice in primary tuberculosis of the breast (which occurs in 70 per cent of the cases) is simple mastectomy together with the usual anti-tuberculous measures. The involved lymph nodes may be treated by dissection or by postoperative irradiation. The *results* are excellent. In secondary tuberculosis the treatment is the same but the prognosis depends entirely upon the type and extent of the systemic involvement.

Plasma Cell Mastitis.—Although not a common lesion plasma cell mastitis is extremely important because it mimics mammary carcinoma. It usually occurs in parous women of an average age of thirty-eight years, but I recently saw a case in a man sixty years of age. The disease is unilateral and in the acute phase it is accompanied by slight redness of the skin, some pain, discomfort, mild tenderness and occasionally a watery or creamy discharge from the nipple. The acute *symptoms* subside in several weeks leaving a localized or diffuse, nontender, hard mass that measures as much as 10 cm. in diameter. It is often adherent to the skin where it produces an orange peel appearance. The nipple becomes retracted and the axillary nodes are usually enlarged and firm. *Grossly*, the lesion is fairly sharply circumscribed but not encapsulated. As a rule it is solid, grayish white, shows numerous, scattered, semi-fluid yellow spots that measure as much as 3 mm. in diameter, and contains grossly visible, dilated ducts filled with semipurulent secretion. The plasma cell *exudate* begins in the ducts, extends through the wall and infiltrates the adjoining tissues in the form of solid sheets and cords (Fig. 61). The duct epithelium first ulcerates and then responds with a proliferative reaction resulting in a piling up of cells to a thickness of eight or ten rows. In addition to plasma

in over one half of the cases and vary in size from 0.3 to 5 cm. in diameter. They may be localized to one duct or extend in a serpentine manner into several adjoining ducts. Their pedicles are single or multiple and thin, broad or sessile. The free intraductal portion is bulbous, of a yellow or hemorrhagic color, has smooth or granular surfaces and is often quite friable. *Histologically*, the tumors are of two main types—those that arise *extraductally* and invaginate into the duct by pushing the lining epithelium before them and those that originate in the ductal epithelium itself. The former consist (1) of thin or broad stalks of richly or poorly vascularized connective tissue that are covered with a single layer of cuboidal epithelium or (2) of distinct glands composed of a single layer of uniform tall cuboidal cells that rest upon a distinct basement membrane. These papillomas are in reality hyperplastic acini that have invaded the ducts from without. They usually contain a scanty stroma that is rich in thin walled, friable capillaries and, like the fibromatous type, they too are covered with a single layer of cuboidal cells that is continuous with the ductal epithelium. Papillomas that arise *within* the ducts are composed of sheets of epithelial cells covering thin, well vascularized connective tissue stalks (Fig. 63). The cells are polygonal, round, oval or spindle, are sharply or ill-defined, have a moderate or scanty cytoplasm, and contain evenly but deeply stained round, oval or spindle shaped nuclei. They are devoid of a covering of cuboidal cells. They bear some resemblance to transitional cell papillomas of the urinary bladder.

A clinical *diagnosis* of duct papilloma is made when there is a history of bleeding from the nipple and when there is no evidence of cystic hyperplasia of the breast or of duct carcinoma. The diagnosis must be confirmed *histologically*. *Treatment* depends upon the type of lesion present. If it belongs to the first group, that is, the fibrous or acinar type that originate *extraductally*, local excision is all that is necessary. Papillomas in this group never become cancerous. If it belongs to the second group, that is those that arise in the epithelium lining of the duct, simple mastectomy is the treatment of choice because these growths may be transformed into a duct carcinoma. In either case the *prognosis* is good.

Fibroadenoma—Fibroadenoma is a relatively common lesion of the mammary gland. It is five times as frequent in females as it is in males, has a peak incidence in each sex at about twenty-three years of age, rarely occurs before puberty or after the menopause, affects nulliparous women more often than those who have borne children, and has a familial tendency in 13 per cent of the cases. Chief *symptom* consists of a lump in the breast of several weeks to many years duration. In one third of the cases there is associated pain of a sharp, dull or burning nature which may be exaggerated before, during or shortly after the menstrual period. The tumor affects each breast with equal frequency, is located in the upper and outer quadrant in over 50 per cent of the cases, is usually single, sharply circumscribed, not tender, round or oval, smooth or lobulated, firm, soft or elastic, and measure from a few millimeters to many centimeters in diameter. When the lesion reaches a large size

sarcoma. Many of the aforementioned tumors are extremely rare and, since their names are self-explanatory, they will not be discussed further. Others, by contrast, are frequent and constitute some of the most common neoplasms in the female. The latter include such benign lesions as duct papilloma, fibroadenoma and cystic hyperplasia and such malignant lesions as Paget's disease, carcinoma and sarcoma. Each of these will now be considered in more detail.

Duct Papilloma.—Duct papilloma of the breast has been described under *many names* some of which are cystosarcoma, cystoma papilliferum mammae, papillary cystadenoma, adenoma, villous papilloma and simply papilloma. It is a tumor confined to the

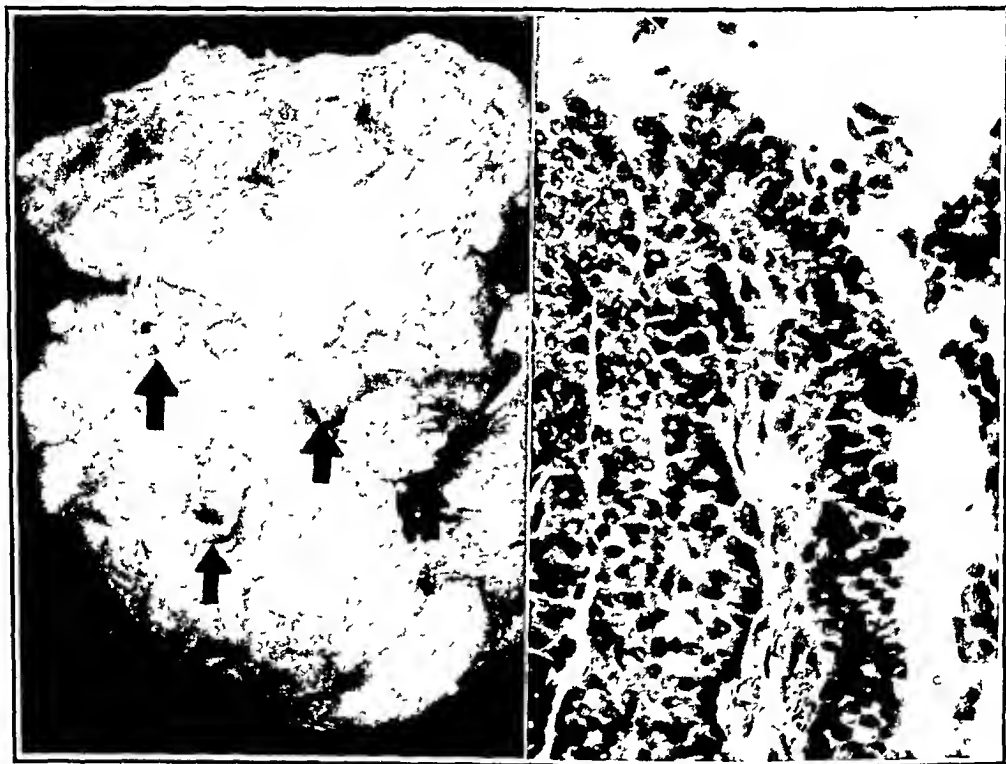


FIG. 62.

FIG 63

FIG. 62.—Ductal papilloma of the breast. The duct and its ramifications are dilated and contain numerous raised, friable growths some of which are indicated by arrows.

FIG 63.—Duct papilloma The epithelial cells are several layers thick and cover well vascularized thin connective tissue stalks. x 200.

excretory ducts and predominates in women after the age of twenty-five years. The only accompanying *symptom* is an intermittent, serous, sero-sanguineous or frankly bloody discharge from the nipple. Physical examination may disclose a small tense or soft tumor in one of the larger ducts beneath the nipple or areola. Often, however, no nodule is palpable but gentle stroking of the involved duct will yield a small amount of discharge.

Grossly, the ducts harboring the tumor are uniformly dilated (Fig. 62). Their walls are thin and when incised they promptly retract beneath the surface of the tumor. Papillomas are multiple

The cause of fibroadenoma is not known. Trauma probably plays a minor role despite its occurrence in 30 per cent of cases in the male and in a fewer number in the female. The most popular theory appears to be a hormonal one. It has been shown that with each menstrual cycle estrogens produce a hyperplasia of the ducts which then differentiate into acini, and that following menses the lobules undergo regression and involution. If there is an excess of estrogens or if the estrogens are normal and the receptor, which in this case is a portion of the breast, is excessively sensitive it is conceivable that hyperplasia will exceed involution resulting in the formation of a



FIG 65

FIG 66

FIG 65—Pericanalicular fibroadenoma. The ducts and alveoli are numerous and hyperplastic. They are surrounded by loose and more peripherally by dense fibrous tissue. $\times 100$

FIG 66—Intracanalicular fibroadenoma. The capsule is dense. The myxomatous connective tissue is over abundant and has drawn out the ducts and alveoli into long slit like processes. $\times 100$

tumor. In support of a hormonal influence are the facts that the tumor rarely occurs before the age of puberty or after the menopause, that it usually starts in adolescence and that in males there is a second smaller peak of incidence in senility. Each of the latter are at a time of greatest hormonal unbalance. A history of the presence of a well circumscribed, solid tumor of long standing ordinarily makes the diagnosis relatively easy, but since no one can be absolutely certain that a solid mammary tumor is not malignant the only logical treatment is surgical excision of the mass. Simple mastectomy may be necessary in large neoplasms that have replaced most of the breast tissue or have become adherent to the skin. The prognosis

the skin and nipple may become adherent and the superficial veins may become considerably distended. Axillary lymph nodes are only occasionally enlarged.

In females the neoplasm is *grossly* sharply circumscribed or encapsulated, but in males the line of demarcation is less definite. Cut surfaces vary according to the type of lesion. In the *pericanalicular* variety they are usually flat, grey and present a whorled appearance but if the connective tissue has undergone myxomatous degeneration they may bulge and appear gelatinous or even somewhat cystic (Fig. 64). In the *intracanalicular* variety the cut surfaces always bulge, are grey and granular, and appear like that of a cauliflower.

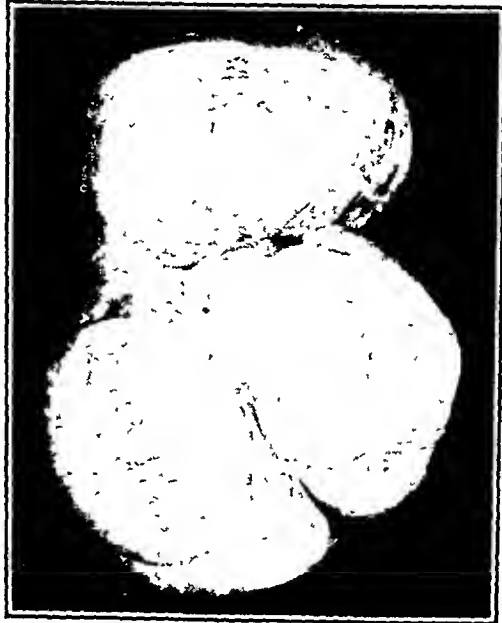


FIG. 64 —Pericanalicular fibroadenoma. There are three well-encapsulated nodules each of which shows a flat, grey somewhat whorled surface.

Calcification occurs in about 1 per cent of fibroadenomas. *Histologically*, the proportion of fibrous to glandular tissue varies and accordingly the tumors are often called fibromas, adenomas, fibroadenomas or adenofibroma. Usually, however, there is always some glandular and some fibrous tissue present so that the terms fibroma and adenoma are not ordinarily applicable. In the *pericanalicular* variety there is an extensive proliferation of both dense and loose myxomatous connective tissue that surrounds hyperplastic and hypertrophied ducts and acini (Fig. 65). The epithelium of the latter, although it may be several layers thick, is always regular. In the *intracanalicular* variety the loose myxomatous connective tissue that normally surrounds acini predominates over the dense interacinar fibrous tissue. As it grows it pushes before it the epithelium of the ducts and acini and draws the lumens out into long, irregular, slit-like spaces (Fig. 66). Whereas a histologic distinction between the two types of fibroadenoma is ordinarily made, one almost always finds a mixture of both varieties in the same tumor. The distinction, furthermore, has no practical significance.

several small, grey, firm, sharply circumscribed or encapsulated nodules that measure 2 or 3 cm in diameter. These are small fibroadenomas. Cysts measuring from less than 1 millimeter to 2 cm in diameter are usually visible throughout the involved area (Fig 67). They are as a rule thin walled and blue to reddish brown in color. They contain clear, pale creamy, grey, tan or deep yellowish brown fluid. Their inner surfaces are usually smooth and grey although occasionally they are rough, pebbled or contain frank papillomatous excrescences. Such areas may indicate the presence of cancer and should be examined with care histologically. Solitary cysts are usually larger and measure as much as 6 cm in diameter. They are discrete, round, movable, tense and frequently appear blue (blue dome). When cut, serous or cloudy fluid escapes under pressure. The lining is silvery grey and smooth.

Histologic changes are diversified and consist of combinations of the following (Fig 68 and 69), (1) An increase of interlobular and

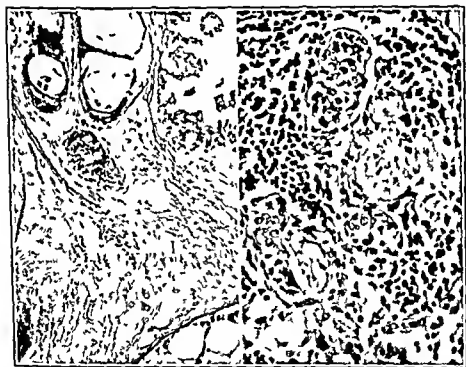


FIG 68

FIG 69

FIG 68—Cystic hyperplasia showing an increase in fibrous tissue, lymphocytic infiltration, hyperplasia of the ductal epithelium and two cysts. One of the latter is lined with attenuated epithelium and the other with large cuboidal eosinophilic cells. $\times 100$
 FIG 69—Cystic hyperplasia. The alveoli are hyperplastic and are surrounded by lymphocytes. $\times 200$

intralobular connective tissue (2) Scattered perilobular and periductal infiltrations with lymphocytic cells (3) A hyperplasia of the acini to form areas that are similar to premenstrual proliferations or to those seen in pregnancy. The lobules are increased in size as a result of an increase in number of acini and the cells are cuboidal,

is good. Recurrences occur in 3.5 per cent of the cases and a sarcomatous change is reported in about 3 per cent of the cases.

Cystic Hyperplasia. This disease has been described under *numerous names* some of which are: chronic mastitis, chronic cystic mastitis, cystic disease, adenocytic disease, mammary dysplasia, adenomatous proliferation, senile parenchymatous hypertrophy, polycystic mammary gland degeneration, mastopathia cystica, cyclomastopathy, fibroadenomatous cystica, cystadenoma mammae and Schimmelbusch's disease. It is perhaps the most common single disorder in women between the ages of thirty and fifty years.



FIG. 67.—Cystic hyperplasia showing two large cysts. The wall between the cysts, indicated by arrows, contains three circumscribed nodules of carcinoma.

It is not seen in adolescence, in pregnancy, in women who have recently borne children or in women with large families, and it rarely occurs after the menopause. The most common *symptoms* are pain, which is never severe but which may be increased during the menstrual period, lumps in the breasts and, in 5 per cent of the patients, a serous or sanguineous discharge from the nipple. Examination discloses the disease to be bilateral more often than unilateral and to involve an entire breast or a portion of a breast. The mammary gland may be tense, tender, indurated, rubbery and firm. There may be numerous shot-like areas scattered throughout the parenchyma or there may be multiple cysts that measure as much as 2 cm. in diameter. If the disease begins at the menopause there often develops a solitary cyst that measures from 3 to 6 cm. in diameter.

Grossly, the parenchyma may be greatly or only slightly increased and it is usually ivory white, pale grey or tan. Often it contains

a complete disappearance of symptoms in the absence of any therapy. Surgical treatment consists of excision of the diseased portion of the gland. The remaining portion should be examined at regular intervals and if cysts or nodules appear a simple mastectomy should be performed. The most serious complication of cystic hyperplasia of the breast is a *cancerous transformation*—a much discussed and controversial subject. The current consensus appears to be that the former does predispose to the latter. The frequency with which a cancerous change takes place, however, is probably less than 10 per cent. Ordinarily the *prognosis* in cystic hyperplasia of the mammary gland is good.

Paget's Disease—In 1871 Sir James Paget reported on a chronic affection of the nipple and areola that was characterized by an intensely red eruption exhibiting finely granular raw surfaces and always associated with a copious, clear, yellowish, viscid exudate.



FIG. 70—Paget's disease of the nipple

Cancer of the mammary gland developed in from one to two years after the appearance of the eczema in every case that he was able to follow. He observed that the neoplasm occurred not in the diseased portion of the skin but in the substance of the mammary gland just beneath the involved area and that the subsequent course did not differ from that of an ordinary carcinoma. The disorder has subsequently been called Paget's disease of the nipple.

Unfortunately, Paget did not confirm his observations histologically. This has resulted in much confusion with regards to the fundamental nature of the disease—a controversy which even today is not completely resolved. The disorder has been considered as (1) a simple dermatitis or eczema, (2) a primary epidermoid carcinoma of the nipple and areola, (3) a carcinoma arising deep in the breast and extending to the surface by growing along the lactiferous ducts and (4) as a primary carcinoma in situ of the superficial portions of the lactiferous ducts with a subsequent intra-epithelial spread both to the surface and to the deeper portions of the mammary gland. The latter theory is currently the most popular and

often vacuolated and several layers thick. (4) *Hyperplasia* of the ducts. The lining epithelial cells are increased in number at irregular intervals. They may be several layers thick, quite regular and maintain their polarity; they may proliferate to fill the entire lumen with solid plugs of deeply stained, large, rather irregular cells, or they may form intraductal papillomas similar to those already described. The appearance of the proliferated cells may be such that the only feature lacking to permit a diagnosis of carcinoma is invasion of the epithelium beyond the confines of the ductal wall. If improperly treated, patients with this type of lesion are prone to develop frank cancer. (5) *Cysts*. These may be microscopic and consist of only slight dilatations of ducts or they may be several centimeters in diameter. The lining cells may be single and cuboidal, flat and attenuated, or large, cuboidal and intensely acidophilic. The latter line the wall in a single row and often form papillary infoldings into the lumen. They appear similar to papillary anhidromas which have already been discussed. (6) *Solid tumor* nodules of intracanalicular and pericanalicular fibroadenoma.

Almost all authors agree that cystic hyperplasia results from a repeated excessive or for that matter a normal parenchymatous hyperplasia that is followed by incomplete involution. The initial cystic spaces are in reality exaggerated vestigial ducts which do not complete their normal differentiation into acini, and the ultimate cysts are formed as a result of stagnation of secretion which is derived from the lining epithelial cells. Most authors also agree that these changes eventuate from hormonal stimuli, but they do not agree upon what *hormone* is at fault or upon the exact mechanism involved. The known facts are (1) that estrogens which are normally secreted by granulosa cells of the Graafian follicle and later by the corpus luteum, are responsible for proliferation of lactiferous ducts, (2) that progesterone, which is secreted by the corpus luteum, is responsible for the differentiation of newly proliferated ducts into acini and (3) that in early cases of cystic hyperplasia progesterone levels are below normal. This allows the unopposed action of estrogens which results in excessive proliferation of ductal epithelium and in a failure of its differentiation into acini. In other words the resulting picture is early cystic hyperplasia. This theory has some experimental confirmation for prolonged estrogenic stimuli in mice will produce not only cystic changes in mammary glands but also adenocarcinoma.

Treatment of cystic hyperplasia has been both hormonal and surgical. The confused state of our knowledge regarding the etiology of this disease has not helped to solve the type of *hormonal* therapy to be employed. Those investigators who presuppose ovarian deficiency as the etiologic agent use estrogens; those who think that the disease results from hyperestrinism employ testosterone propionate, and those who consider a deficiency of corpus luteum hormone as the cause use progesterone. The objections to endocrine therapy are that estrogens may foster the development of carcinoma, that beneficial results are only temporary, and that the disease is characterized by spontaneous remissions with frequently

the least common cancers in men. Ninety-nine per cent of cases are found in females and only 1 per cent in males. Both clinically and pathologically, however, the disorder is similar in both sexes. Thus although the following remarks are primarily directed toward the disease in women most of them are also applicable to the disease in men.

The peak incidence of carcinoma of the breast is between the ages of forty-one years and forty-five years. It is infrequent before the age of thirty years, is rare before the age of twenty years, but it may arise at any time after the menopause. The most common *symptom* is a painless lump in the breast of a few weeks, of several months or, less often, of several years duration. The only other early symptom of note, in a minority of patients, is a bloody discharge from the nipple. The *tumor* affects each breast with equal frequency and is found in the upper and outer quadrant of the mammary gland in almost one half of the cases and in the upper and inner quadrant and central portion of the breast in an additional quarter. The mass is usually single and unilateral but the disease may be of multicentric origin and, concomitantly or in succession, it may involve both breasts. The shape and size of the tumor and the appearance of the adjacent tissues depend not only upon the duration of the neoplasm but also upon the type of cancer. Some tumors, as for example scirrhous carcinoma, rarely attain a size larger than 2 to 4 cm in diameter whereas others, such as inflammatory carcinoma, grow to 20 cm in diameter within a few weeks. Generally speaking, however, they vary in size from 1 to 10 cm. They are solid and moderately firm or hard, but, rarely, they may be cystic. Early the lesions are freely movable whereas later they are attached not only to the skin and fascia but also to the underlying muscle and thoracic cage. The *covering epidermis* becomes thinned, stretched and finally breaks down and ulcerates. If the tumor spreads rapidly the superficial lymphatics become blocked, edema develops in the skin, the hair follicles become accentuated and the skin assumes a typical orange peel (*peau d'orange*) appearance. If, in addition, the subpapillary capillaries are blocked there is stasis of blood resulting in a blush or a fiery red discoloration of the involved integument. A diffuse permeation of subepithelial lymphatics produces a uniform infiltration of the subepidermal tissue with cancer cells with the formation of a sheet of cancerous tissue that encases a whole breast, both breasts or even the entire anterior portion of the thorax (cancer en cuirasse). *Retraction of the nipple*, resulting from permeation of lymphatic vessels and ducts with carcinoma cells, is a common sign in some types of cancer that arise beneath or near the areola. Finally, physical examination frequently reveals enlarged firm lymph nodes in the axilla and, in more advanced cases, in the supraclavicular region.

From both a clinical and a pathologic point of view, carcinoma of the breast may be conveniently divided into the following *five types*, scirrhous, medullary, comedo, inflammatory and mucinous. *Other histologic forms* of the disease that have been described are carcinoma in situ, sweat gland carcinoma, squamous cell carcinoma,

has recently been substantiated by several excellent histopathologic studies.

The disease occurs in women beyond the age of fifty years and is usually unilateral. The chief *complaint* is a chronic eczema of the nipple of one to several years duration which in some cases is followed by a lump in the breast of several months duration. Occasionally the sequence of events is reversed. *Grossly*, the lesion may involve the nipple, the areola, or both of these structures, and if it is of long duration it extends to the surrounding skin (Fig. 70). *Histologically*, the characteristic cell is large, edematous, usually round, vacuolated and exhibits a small shrunken, deeply stained or a large vesicular nucleus (Fig. 71). It is found within the epithelium

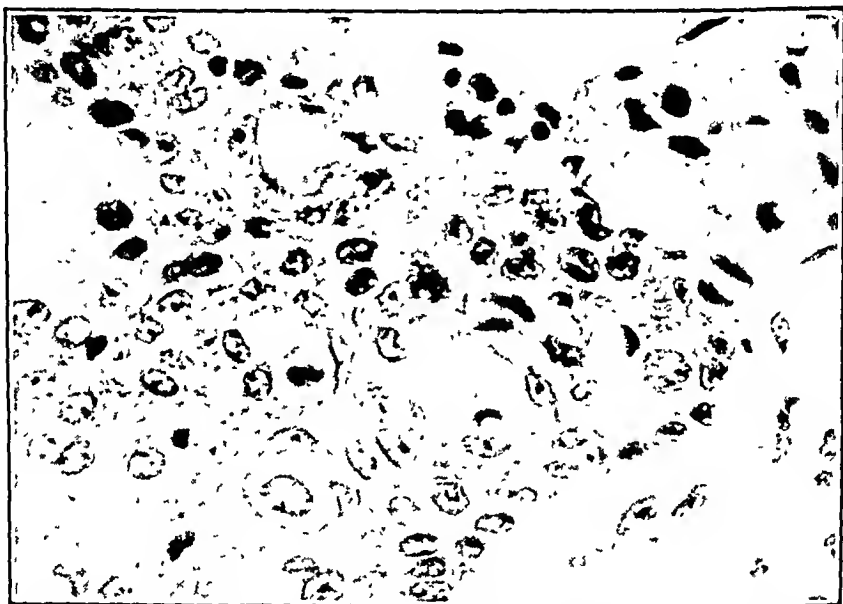


FIG 71 —Paget's disease of the nipple showing several typical large clear intra-epithelial Paget's cells x 400.

of the nipple and areola, within the epithelium of the lactiferous ducts and in the adjoining breast substance itself. In early cases there are in addition hypertrophy of the epithelium and subepithelial round cell infiltration. As the lesion progresses it develops into an outright ductal carcinoma that infiltrates the adjoining breast parenchyma, that metastasizes to distal organs and that histologically is indistinguishable from any other ductal carcinoma of the mammary gland.

A *diagnosis* of Paget's disease should be made in any patient with chronic eczema of the nipple or areola that does not respond to local therapy. Since the disease is cancerous from the start the accepted *therapy* is radical mastectomy. The *prognosis* depends upon the extent of the lesion. If it is confined to the skin without a grossly detectable intramammary tumor the outcome is generally good. In the presence of a mass in the breast it is only fair and when there are metastases the prognosis is poor.

Carcinoma.—Carcinoma of the mammary gland is the most common malignant tumor in women and, conversely, it is one of

of a green pear and the cut surface is always depressed beneath the level of the surrounding tissue (Fig 72). The neoplasm is greyish white and contains throughout its substance small, yellowish foci. The borders are irregular, ill-defined and blend imperceptibly with the adjacent mammary parenchyma. *Histologically*, there are varied proportions of epithelial cells and fibrous tissue. At one extreme epithelial cells predominate and at the other extreme fibrous tissue overshadows all other elements (Fig 73). Epithelial cells are uniformly or irregularly distributed throughout the tumor in the form of sheets, strands, nests, small cords, acini or single cells. The individual cells vary in shape and size but are not large. The cytoplasm is usually ill-defined, abundant to scanty, eosinophilic and solid or vacuolated. The nuclei are of all shapes and sizes. They are hyperchromatic, pyknotic or vesicular and are rarely in a state of mitosis. The supporting stroma is always dense, fibrotic and acellular. Usually it is free of inflammatory cells but it may contain foci of lymphocytes and plasma cells. Blood vessels are inconspicuous and foci of necrosis are uncommon.

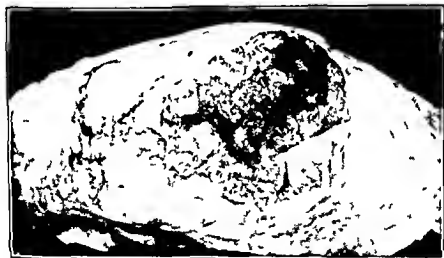


Fig 74—Medullary carcinoma. The tumor is bulky, moderately firm, encephaloid and shows a central area of necrosis and hemorrhage.

Medullary Carcinoma—This, the second most common type of mammary cancer, accounts for about one sixth of all cases. Unlike the scirrhous type it grows rather rapidly and the patient usually presents herself with a bulky tumor that measures 5 cm. or more in diameter. *Grossly*, the neoplasm is roughly round but irregularly lobulated. It is sharply circumscribed although not encapsulated and on section it presents a soft, greyish white, bulging surface that often contains irregular areas of necrosis and hemorrhage (Fig 74). In large tumors the overlying skin is stretched, thin and often ulcerated. It does not present the dimpling that is so frequently seen in scirrhous carcinoma.

Histologic sections disclose anastomosing solid sheets or broad strands of cancer tissue. The cells are of moderate size or quite

and adenosarcoma. These, however, are too infrequent to merit further discussion. Despite various classifications and minute histologic subdivisions it should be pointed out that most, if not all, mammary carcinomas probably *arise* from basal cells of the ductal epithelium. The most frequent point of origin is at the site where ducts normally proliferate to form acini but the neoplastic process may originate anywhere along their course. The ultimate histologic pattern will be determined by further differentiation or lack of differentiation of the tumor cells and by their ability to stimulate connective tissue to proliferate. Since these factors do not operate uniformly throughout all parts of the same tumor one, more frequently than not, encounters various combinations of the types to be described not only in different parts of the same neoplasm but even in a single histologic section.

Scirrhus Carcinoma.—This, the most common type of mammary cancer, accounts for about two thirds of all cases. Its average size

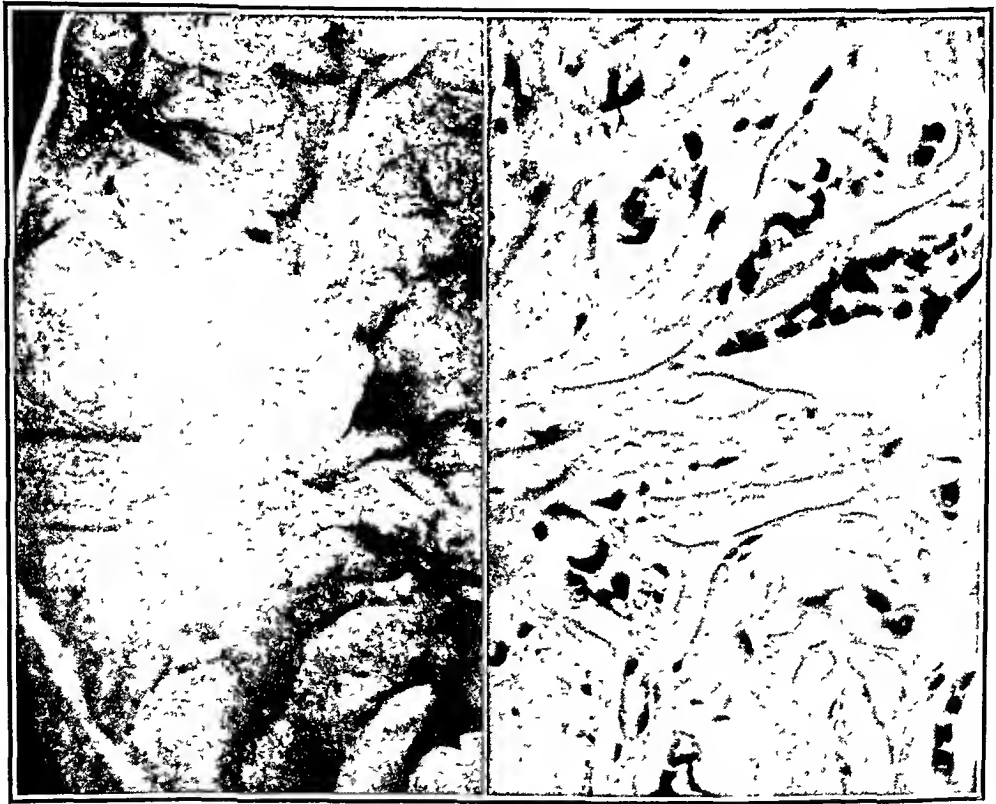


FIG 72.

FIG 73

FIG 72 —Scirrhus carcinoma The tumor is ill-defined and the surface is depressed beneath the level of the surrounding tissue

FIG. 73.—Scirrhus carcinoma showing islands of epithelial cells surrounded by dense, acellular fibrous tissue x 200.

is approximately 2 cm. in diameter; it rarely exceeds 4 cm., and it often measures only a few millimeters across. Despite the small size, permeation of lymphatics is frequent, and both retraction of the nipple and orange peel appearance of the skin are common accompaniments. The *tumor* is hard to palpation and from this it derives its name (skiros meaning hard). It cuts with the resistance

tumors are fairly well circumscribed while others are less sharply delineated. The most characteristic gross feature is the presence of small yellowish foci set in grey tumor tissue which upon compression are readily expressed in a manner similar to comedones. Microscopic sections disclose solid cords of cancer cells plugging mammary ducts (Fig 77). Central or peripheral foci of degeneration to complete necrosis with often superimposed erythrocytic extravasation are common. The cells are large irregular and have indistinct borders. The cytoplasm is abundant basophilic or slightly eosinophilic, usually solid and sometimes vacuolated. The nuclei are round, oval, spindle or irregular. The nucleoplasm is clumped and deeply stained and mitoses are numerous. When infiltration of the adjacent stroma occurs cancer cells are found in solid cords that appear similar to those filling the ducts or they



FIG 77.—Comedo carcinoma. Three ducts are plugged with cancer cells. In one the tissue is solid whereas in two the centrally located cells are necrotic. $\times 200$

closely resemble those seen in ordinary scirrhous and medullary carcinoma. In all cases the supporting stroma is composed of dense, acellular, fibrous tissue and it is either abundant or scanty. Scattered throughout the tumor there are foci of lymphocytes and fewer numbers of plasma cells.

Inflammatory Carcinoma—Inflammatory carcinoma has been described under various names some of which are acute brawny cancer, acute scirrhous carcinoma, acute medullary carcinoma, inflamed cancer and lactation cancer. While it constitutes only about 3 per cent of all mammary cancers it is important firstly, because it is sometimes extremely difficult to differentiate this lesion from acute mastitis and secondly, because the disease is universally fatal. The history is quite characteristic. The initial symptom is a lump in a lactating or non-lactating breast that enlarges rapidly so that in a few weeks the entire mamma is two or

large. They are oval, round or polyhedral and are irregularly arranged throughout but sometimes those at the periphery are placed at right angles to the main mass (Fig. 75). The cell boundaries are distinct or ill-defined. The cytoplasm is usually basophilic and solid although sometimes it is slightly acidophilic and may be reticulated or vacuolated (Fig. 76). The nuclei vary considerably in shape and size. They are round, oval, spindle or otherwise irregular and are hyperchromatic or vesicular. Nucleoli are occasionally conspicuous and mitoses are usually abundant. The supporting connective tissue is scanty, cellular and vascular. Fre-

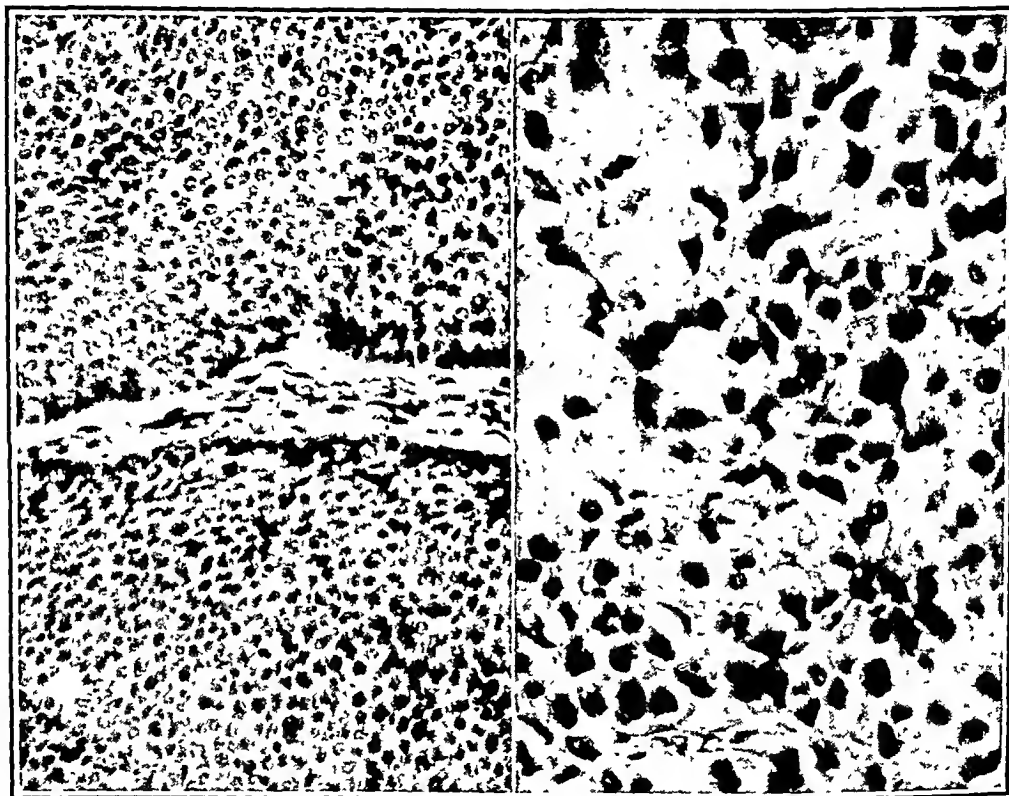


FIG. 75

FIG. 76

FIG. 75 —Medullary carcinoma showing solid sheets of cancer cells. The cell borders are indistinct, the cytoplasm is basophilic and the nuclei are round, oval and deeply but evenly stained. $\times 200$

FIG. 76 —Medullary carcinoma. The cells are large and irregular, and the cytoplasm is reticulated or vacuolated and eosinophilic. Mitoses are numerous. $\times 200$.

quently it is edematous and it may be infiltrated with lymphocytes and plasma cells. While in smaller tumors most of the tissue is viable in bulky neoplasms there are large areas of complete necrosis and erythrocytic extravasation.

Comedo Carcinoma.—This type of carcinoma constitutes about 5 per cent of all mammary cancers. It is the most common malignant tumor that produces bleeding from the nipple. It arises in all portions of the ducts but is more common in those of intermediate size. Ordinarily the tumor is larger than a scirrhous carcinoma but does not reach the dimensions of a medullary cancer. In consistency it is usually softer than the former but harder than the latter. Some

Mucinous Carcinoma—Mucinous carcinoma of the mammary gland has also been called colloid, gelatinous, mucoid and myxomatous cancer. It constitutes about 2 per cent of all carcinomas of the breast and is found on an average between the ages of forty-six and fifty years. The chief *symptom* is a painless lump usually located in the upper and outer quadrant or in the central portion of the mamma that grows slowly over a period of months or years. Sanguineous discharge from the nipple is present in 10 per cent of the cases. Physical examination reveals a small tumor when compared with the duration of symptoms. If the lesion is near the areola, the nipple may be both enlarged and protruding rather than retracted. In neoplasms of short duration the mass is firm and solid but in those of longer duration it is often cystic. *Pathologically*, this type of cancer is dividable into two groups, (1) true mucinous carcinoma and (2) *mucinous degeneration* of an ordinary cancer. The latter is often a medullary or a comedo carcinoma with foci of mucinous degeneration which may be seen grossly but are at times found only microscopically. *True mucinous carcinoma* is sharply circumscribed, often well encapsulated and measures from 2 to 22 cm. in diameter. Cut surfaces disclose either a solid mass of glistening, light grey, semi-transparent gelatinous tissue or a cyst composed of a well-defined capsule of fibrous tissue and filled with stringy semifluid material or old blood (Fig. 80). The *histologic* structure varies according to the degree of mucinous change. In true mucinous carcinoma, with which we are concerned here, the bulk of the tumor is composed of large collections of basophilic, stringy material in which there are small, solid or cystic collections of cancer cells (Fig. 81). The latter are of a moderate size, have indistinct borders and solid or vacuolated, eosinophilic cytoplasm. The nuclei are small, irregularly shaped and hyperchromatic and more vesicular. The supporting stroma is composed of anastomosing cords of dense fibrous tissue which sometimes contain foci of calcification and ossification.

Spread of carcinoma of the breast occurs by direct extension, by way of lymphatics and by way of blood vessels. As already noted, *local extension* involves first the adjacent mammary parenchyma and only in advanced cases does it affect the integument and muscles of the thoracic cage. The rapidity with which the latter two develop varies with the type of cancer. Thus in mucinous carcinoma ulceration of the skin may not occur in tumors of five to ten years' duration, whereas in inflammatory or medullary carcinomas it may develop a few weeks or a few months after the first appearance of the lesion. Spread of cancer by *lymphatics* usually occurs by means of emboli that are carried intraluminally in the direction of lymph flow. Once the lumen is blocked, however, the direction of lymph flow is reversed and retrograde metastasis is a common feature. It is by the latter mechanism that the integument is usually affected in cancer en cuirasse and in those cases producing an orange peel appearance of the skin. It is also by retrograde lymphatic metastasis that the neoplastic process ordinarily spreads to the second breast. Usually, however, tumor cells are carried with the lymph

three times the normal size. There are in addition pain, redness, swelling, heat, tenderness, orange peel appearance to the skin, and a rapid involvement of the axillary and supraclavicular lymph nodes. Death may occur as early as six weeks after the onset of symptoms. *Pathologically*, this is not a distinct type of tumor but rather it is any cancer of the breast that grows rapidly and is accompanied by pain, tenderness, heat and redness of the skin. There are, therefore, two circumstances under which this chain of events may occur. (1) When there is extensive and rapid tumor cell permeation of the subepidermal lymphatic vessels and capillaries resulting in stasis of blood. This produces the conventional signs of inflammation.

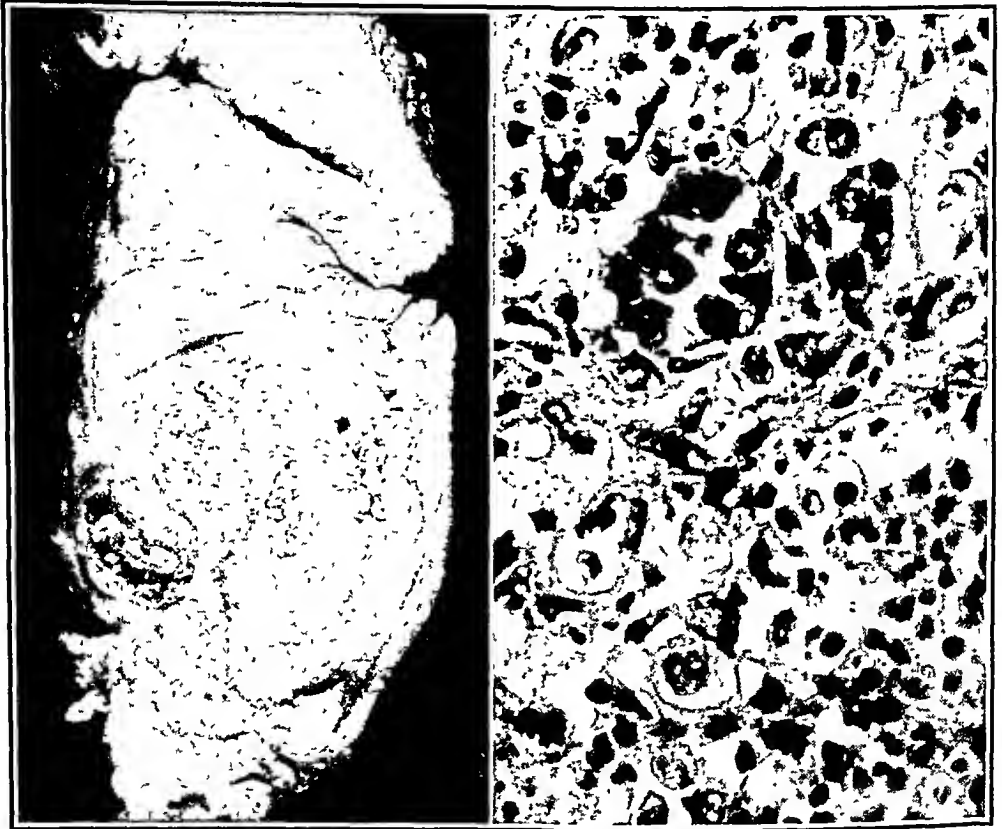


FIG. 78

FIG. 79.

FIG. 78.—Inflammatory carcinoma. The tumor is bulky, encephaloid and shows areas of necrosis.

FIG. 79 —Inflammatory carcinoma showing an intermingling of large irregular neoplastic cells and neutrophils. $\times 400$.

(2) When a tumor, either from the onset or at a later date, is accompanied by an actual leukocytic infiltration which eventuates in signs of inflammation. *Grossly*, therefore, the neoplasm varies considerably in appearance. Because of its rapid growth, however, it often resembles rather closely a medullary carcinoma (Fig. 78). The *histologic* pattern is that of a medullary, comedo, scirrhus or mixed type of carcinoma. In addition, the subepidermal lymphatic vessels are almost always filled with cancer cells and, in some of the cases, there is an admixture of both cancer cells and leukocytes chief among which are neutrophils (Fig. 79).

and this may be present long before there is any roentgen evidence of bone destruction. In a minority of cases a pathologic fracture is the first indication that something is amiss. Any bone in the body may be the seat of metastasis although those with red marrow, and particularly the vertebrae and pelvis, are most frequently affected, whereas the bones distal to the knee and to the elbow are rarely involved. In approximately 75 per cent of the cases the osseous lesions are osteolytic, in 5 per cent they are osteoblastic and in 20 per cent they are both osteolytic and osteoblastic.

The causes of mammary carcinoma in man are not definitely known, yet the massive data that have gradually accumulated inescapably point to at least two etiologic factors namely, heredity and hormones. That a *hereditary* predisposition for carcinoma exists has been established (1) by the fact that certain races are more prone to cancer of the breast than others, as for example, Europeans as compared with Japanese, (2) by the fact that women of several successive generations have been known to develop mammary carcinoma—sometimes even of the same breast and (3) by the occasional occurrence of the disease in homologous twins. Ovarian hormones doubtlessly play an important causative role in the development of cancer of the breast for the disease does not occur before puberty and its incidence in males is only 1 per cent. In each of these instances the mamma is rudimentary and it appears, therefore, that preliminary ovarian stimulation is a prerequisite for the evolution of carcinoma. Further support for this statement lies in the fact that cystic hyperplasia and other benign lesions of the breast (which result from ovarian over-stimulation) predispose to mammary cancer. The experimental approach to the problem has been most fertile. It has been proved that the factors necessary for the development of mammary tumors in mice consist of (1) an inherited susceptibility, (2) hormonal (estrogenic) stimulation, (3) an active agent transmitted through milk and (4) environment as, for example, diet, temperature and overcrowding.

The *diagnosis* of carcinoma of the breast is easy, if one remembers the dictum that any solid tumor of the mamma is cancer until proved otherwise. And the only way that one can prove that a lesion is benign, is to remove it surgically and to study it histologically either by frozen section or routine paraffin technique. The only effective *treatment* is radical mastectomy. Unfortunately this has limitations and to be successful the lesion must be removed early. Formerly, the criteria for operability and inoperability have been rather fluid, but recently, they have been rigidly set forth by Haagensen and Stout. Their scholarly article is recommended to the interested reader. In advanced cases, which can not or should not be operated upon, irradiation therapy, castration or administration of testosterone propionate has a salutary effect. These forms of therapy are of particular value in patients with bony metastases. Not only does pain disappear but, in some cases, the metastatic lesion decreases in size and the bone recalcifies. The *prognosis* in carcinoma of the breast should always be guarded for reported five year survival rates range only from 22 to 49 per cent.

to the first chain of lymph nodes, to larger lymphatic channels and ultimately into the blood stream. Generally speaking, the regional nodes most commonly affected are those which drain that portion of the breast wherein the tumor lies. Thus, since the upper and outer quadrant of the mamma is the usual site of the neoplastic process, the lymph nodes in the axilla are most frequently involved. The supraclavicular, and abdominal nodes are affected in proportion to the frequency with which the upper, medial or infero-medial portions of the breast are affected by cancer. It must be emphasized, however, that these anatomical distributions are not always strictly adhered to firstly, because cancer is often not limited to one

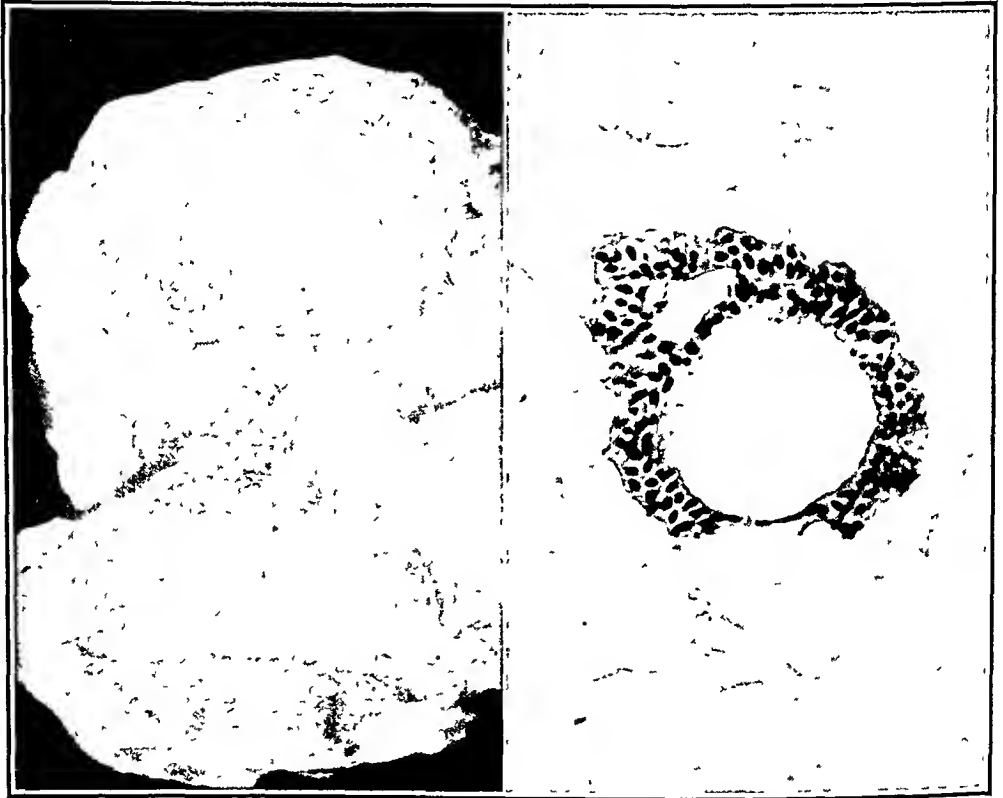


FIG. 80.

FIG. 81.

FIG 80.—Mucinous carcinoma The tumor is fairly well-circumscribed, of a glistening gelatinous appearance and reveals two foci of necrosis and hemorrhage

FIG 81 —Mucinous carcinoma showing a cystic collection of neoplastic cells surrounded by abundant stringy mucinous material. x 200

sector of the breast and secondly, because a rich lymphatic anastomosis permits the retrograde spread of tumor in every direction.

Metastasis by the *blood stream* results in spread of carcinoma to the same breast, to the opposite breast or to distant parts of the body. In decreasing order of frequency the organs and tissues affected are; lungs, liver, bones, distant lymph nodes, skin, pleura, adrenal glands, spleen, ovaries and brain. In women, cancer of the breast is the most common of all metastatic tumors to bones. *Osseous dissemination* may already be present when the original lesion is first noted or it may occur many years after the primary tumor has been eradicated. The most common symptom is pain

bulging, greyish white and often myxomatous. The intracanalicular variety is frequently traversed by deep clefts or spaces and is cystic whereas the pericanalicular variety is solid and more whorled in appearance. The histologic pattern varies from that which approaches a normal fibroadenoma to that which resembles a frank fibrosarcoma (Fig 83). The epithelial cells may show some hyperplasia or metaplasia but ordinarily their presence is merely passive. The connective tissue cells, however, show only a myxomatous transformation or they are quite cellular, spindle, pleomorphic, hyperchromatic and disclose numerous mitoses. Despite their rapid increase in size and histologic appearance these neoplasms usually pursue a benign course although a few have been known to produce



FIG 83

FIG 84

FIG 83—Adenofibrosarcoma showing a slit like elongation of a duct with bizarre connective tissue cells on one side and relatively regular fibrous tissue on the other $\times 200$

FIG 84—Fibrosarcoma. The tumor is composed of interlacing bundles of spindle cells exhibiting scanty basophilic cytoplasm and relatively large, deeply stained, spindle nuclei $\times 200$

metastases. *Treatment* consists of wide local excision or, if the tumor is large, of a simple mastectomy. The *prognosis* is good.

Fibrosarcoma—This tumor is separated from the foregoing because it does not arise in a previous fibroadenoma and because it tends to recur locally and to metastasize more frequently than does adenofibrosarcoma. It can occur at any time from birth to senility, but the most common age is from thirty-five to sixty-five years. *Clinically*, the tumor starts in a previously normal breast and enlarges slowly and progressively, but as a rule does not attain the large size so commonly found in adenofibrosarcoma. It is round or oval, sharply circumscribed, firm and not cystic. *Cut surfaces* are diffusely greyish white or light pink and of the appearance and consistency of brain tissue. In larger tumor they often exhibit foci of necrosis and hemorrhage.

and permanent arrests are considerably fewer. The *average duration* of the disease from onset to death is about three years.

Sarcoma.—The incidence of sarcoma of the breast varies, according to different observers, from 0.5 to 7.7 per cent of all malignant mammary tumors. Most of the recorded cases have been found in women. As already noted in the opening paragraph of the section on neoplasms of the breast, all mesodermal tissues normally present, and some that are not normally present, in the mamma have been known to give rise to a sarcomatous tumor. The only two, however, that are common enough to warrant further consideration are adenofibrosarcoma and fibrosarcoma.

Adenofibrosarcoma.—The *synonyms* for adenofibrosarcoma are cystosarcoma phylloides, cystosarcoma and cystosarcoma proliferum.



FIG. 82—Adenofibrosarcoma The tumor is encapsulated, bulky and shows some cystic degeneration

This tumor arises as a sarcomatous change in a pericanalicular or an intracanalicular fibroadenoma of the breast. It may occur at any time after puberty but the peak incidence is the fifth decade of life. The usual *history* is the presence of a lump in the breast for several years which suddenly, during gestation, lactation, after trauma or spontaneously, begins to increase in size rapidly. The *lesion* is ordinarily single and unilateral but, rarely, it is multiple and bilateral. The involved breast is always larger than its mate; the nipple is protruberant rather than retracted, and the skin covering the tumor is thin and sometimes ulcerated. The mass is globoid, lobulated, firm or cystic, freely movable and measures from 4 to 20 cm. in diameter. Grossly, the neoplasm is usually encapsulated or at least sharply circumscribed (Fig. 82). Cut surfaces are

incidence It occurs in middle aged, obese women, with pendulous breasts Usually the only complaint is a painless lump in the breast which may or may not have been preceded by trauma Examination reveals a stony hard, round, or irregularly circumscribed, mass that measures as much as 2 cm in diameter The skin is adherent to the tumor in 50 per cent of the cases, and the nipple is retracted in 10 per cent Initially, the lesion is sharply circumscribed, opaque, solid and chalky white Soon central foci of liquefaction appear and the cavities are filled with oily fluid or greasy debris With increase of fibrous tissue the entire mass becomes diffusely greyish white and takes on the appearance of a carcinoma The histologic changes consists of (1) a breaking down of fat cells to form larger spaces, (2) a surrounding inflammatory reaction of neutrophils followed by, monocytes, foam cells, plasma cells, lymphocytes, and foreign body giant cells, (3) an increasing proliferation of adjacent fibrous tissue, (4) a transformation of some of the fat into crystal like spaces, (5) an obliterative endarteritis, and (6) the formation of cystic spaces surrounded by dense fibrous connective tissue with often areas of calcification The lesion results from simple trauma, injection of foreign material as for example fats, oils or simple fluids, following mastectomy, and after infection The exact mechanism is in doubt but the assumption is that the aforementioned disturbances first produce simple ischemic necrosis which secondarily is acted upon by enzymes liberated from the blood or fat cells and by lipase which is normally present in blood Treatment is local excision followed by frozen section examination, for otherwise no one can be certain that the lesion is not cancerous The prognosis is excellent

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Microscopically, they vary from well differentiated cellular fibromas to completely anaplastic and pelomorphie sarcomas (Fig. 84). The latter consist of spindle, round or tumor giant cells with scanty basophilic cytoplasm and spindle, round or irregular, piled up intensely hyperchromatic nuclei. There may be varying degrees of myxomatous change and metaplastic foci of malignant chondroid or osseous tissue. A *diagnosis* of fibrosarcoma can only be established histologically although from the history and gross appearance of the lesion one can be reasonably certain that the tumor is malignant. Since metastasis is by the blood stream wide local excision or mastectomy with removal of the underlying muscle, rather than a radical amputation of the breast, is the *treatment* of choice. The *prognosis* is better than it is in carcinoma of the mammary gland.

Mechanical Disturbances.—Bleeding from the Nipple.—Bleeding from the nipple is, of course, a symptom and not a disease entity. A woman will often nurture a lump in the breast for weeks or months but a sanguineous discharge from the nipple usually causes her to seek medical advice early. It is an infrequent complaint occurring only in 6 per cent of cases admitted to the hospital because of symptoms referable to the mamma. Its three most common *causes* are duct papilloma, carcinoma and cystic hyperplasia. Other rarely reported causes are simple dilatations of the ducts, inflammations, trauma, hormonal dysfunction, Paget's disease and sarcoma. Benign lesions account for 60 per cent of cases and malignant ones for 40 per cent. Usually the discharge comes from a single duct but sometimes it escapes from several openings. *Examination* may or may not reveal a palpable tumor in the nipple or beneath the areola. Of aid in the localization of the lesion are (1) careful finger-tip pressure upon the various segments of the mamma in an endeavor to express a discharge from a duct or ducts, (2) transillumination; A duct filled with blood will appear dark and (3) mammography, that is, roentgenograms of the breast following an intraductal injection of radio-opaque material. Because of occasional severe tissue reactions this method has not gained universal favor. The ultimate *diagnosis* rests with a careful histologic examination of the lesion. This can not be performed satisfactorily by the frozen section method because the transition from a benign to a malignant lesion is often subtle and by this technique the tissue crumbles upon cutting and the sections are too thick for a proper evaluation. *Treatment* of benign lesions is local excision of the involved duct and segmental resection of the corresponding sector of the duct or, if bleeding results from cystic hyperplasia and the disease is advanced, it consists of simple mastectomy. Treatment of malignant lesions is radical mastectomy. The *prognosis* depends on the cause of the symptom. In benign lesions it is excellent; in cancerous ones it should be guarded.

Fat Necrosis.—Fat necrosis of the breast is not a common lesion but it is extremely important because it mimics carcinoma. Some of the *other names* under which it has been described are saponifying necrosis, traumatic fat necrosis, ischemic fat necrosis and lipogranulomatosis. There is no way of accurately determining its

Chapter III

NOSE AND SINUSES

EMBRYOLOGY

THE upper portion of the respiratory tract consists of the nose, the paranasal sinuses and the pharynx. Since the latter also forms part of the upper digestive system and is intimately bound with its development, it is considered in connection with the mouth. The nose is first identified in the 4 mm embryo as two thickenings of ectoderm covering the ventrolateral surface of the head and known as olfactory plaques. In each, a groove-like depression of the central and ventral portion and simultaneous elevation of the medial and lateral borders, produce respectively the olfactory pit and the medial and lateral nasal processes. Ultimately, fusion of the medial nasal processes with each other and with the maxillary processes results in the formation of the upper jaw and fusion of the lateral nasal process with the adjacent portion of the maxillary process completes the formation of the cutaneous opening of the nose. This is now called the *external nares*. An epithelial plate separates the deep end of the olfactory sac from the mouth until the seventh week of embryonic life when the membrane perforates to form the primitive choana. With growth of the posterior portion of the head the olfactory pits assume a more midline position and the tissue between them is compressed to form the nasal septum. A part of the upper portion of the primitive mouth is incorporated into the nose by the transverse growth and union of the palatine processes. Meanwhile the caudal extension of the septum and its fusion with the palate completes the formation of the two nasal passages which now open into the pharynx by permanent choanae or the *posterior nares*. The lining of the superior portion of the nasal passage develops nerve cells which assume an *olfactory* function whereas that of the inferior portion remains as *respiratory epithelium*. Outfoldings of the mucosa of the lateral wall into the nasal cavity become supported first by cartilage and then by bone and form the superior middle and inferior *conchae*. The *paranasal sinuses* are first evident at approximately the fourth month of embryonic life as foci of bone destruction that are invaded by the overlying nasal epithelium. The ethmoid and maxillary sinuses are well developed at birth, but the frontal sinuses are not pneumatized until after birth and the sphenoid sinuses not until the third year.

ANATOMY

Gross Anatomy—The nose is roughly pyramidal in shape. Its junction with the forehead is called the *root*, its free angle the *apex*, its superior lateral surface the *dorsum nasi* and its inferior lateral surface the *alae nasi*. The *base* is that portion which contains the

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Microscopic Anatomy—The *vestibule* is lined with regular stratified squamous epithelium. The *respiratory epithelium* like that in the nasopharynx, larynx and trachea is composed of pseudostratified ciliated columnar cells interspersed with which are goblet cells (Fig 85). The mucosa rests upon a distinct basement membrane. A submucosa or *tunica propria* composed of loose connective tissue contains a few fat cells, mixed mucous glands, nerves, blood capillaries and lymphatic channels (Fig 86). The inferior conchae and the inferior part of the septum are particularly rich in a venous plexus whose function it is to warm the air. The *olfactory epithelium* is pseudostratified columnar and lacks a distinct basement membrane. It consists of three types of cells: (1) long slender supporting columnar cells whose free borders end in cuticular plates, (2) conical basal cells with branching processes and dark nuclei, and (3) olfactory cells which are in reality bipolar nerve cells. The olfactory glands are of the branched tubulo-alveolar type the secretory portions of which are lined with cuboidal cells containing secretory granules. The lining of the *para-nasal sinuses* is similar to that of the nasal cavity with the exception that glands are scarce and that the *tunica propria* is closely adherent to the periosteum (Fig 85).

PATHOLOGY

Congenital Anomalies—Arrest of growth at various stages of embryonal development accounts for the following abnormalities of the nose: complete *absence* except for an aperture, *deformity* of one side, *bifid apex*, *double nose*, *stenosis* or *atresia* of both the external and internal *naris*, an incomplete, deviated, displaced or broad *septum*, large, small or misshaped *conchae*, *cleft palate*, and congenital cysts. The latter consist of fissural cysts, dermoid cysts and encephalomeningoceles. Fissural cysts result from inclusions of epithelial cells in the lines of fusion that eventuate from the coalescence of the component parts of the upper jaw. They affect females more often than males, are usually unilateral but may be bilateral, may not become manifest until adult life and present as cystic swellings in the lateral or medial side of the floor of the nose. The lumen of the cyst contains mucus and cholesterol and the wall is lined with ciliated epithelium that shows marked goblet cell activity.

Dermoid cysts are also developmental in origin and although they may be present at birth, they are usually not noted until ten to twenty years later. They occur anywhere from the root to the apex of the nose and arise from embryonal inclusions of ectodermal tissue. The usual symptom is a cystic swelling but sometimes as a result of infection, the surface may be broken and the lesion exists as a draining sinus. The wall is lined with keratinizing stratified squamous epithelium and contains hair and sebaceous and sweat glands (Fig 87). Encephalomeningomyeloceles are midline, cystic herniations of the brain and meninges through the frontal or ethmoid bones. They arise in early embryonic life as an outgrowth from the anterior cerebral vesicle. Later the membranous skull is laid

external nares. The *vestibule* is the first part of the nasal cavity situated just inside the nares. It is bounded laterally by the ala and contains a filter of hairs. As already stated the lateral wall harbors three *conchae*, below each of which there is a recess called respectively the superior, middle and inferior *meatus*. The lateral wall also contains the openings of the corresponding paranasal sinuses. The *frontal sinus*, situated in the frontal bone and measuring 3.2x2.6x1.8 cm., opens into the anterior part of the middle meatus. The *ethmoid sinuses*, located between the upper part of the nasal cavity and the orbit consist of anterior, middle and posterior cells. The anterior and middle cells open into the middle meatus

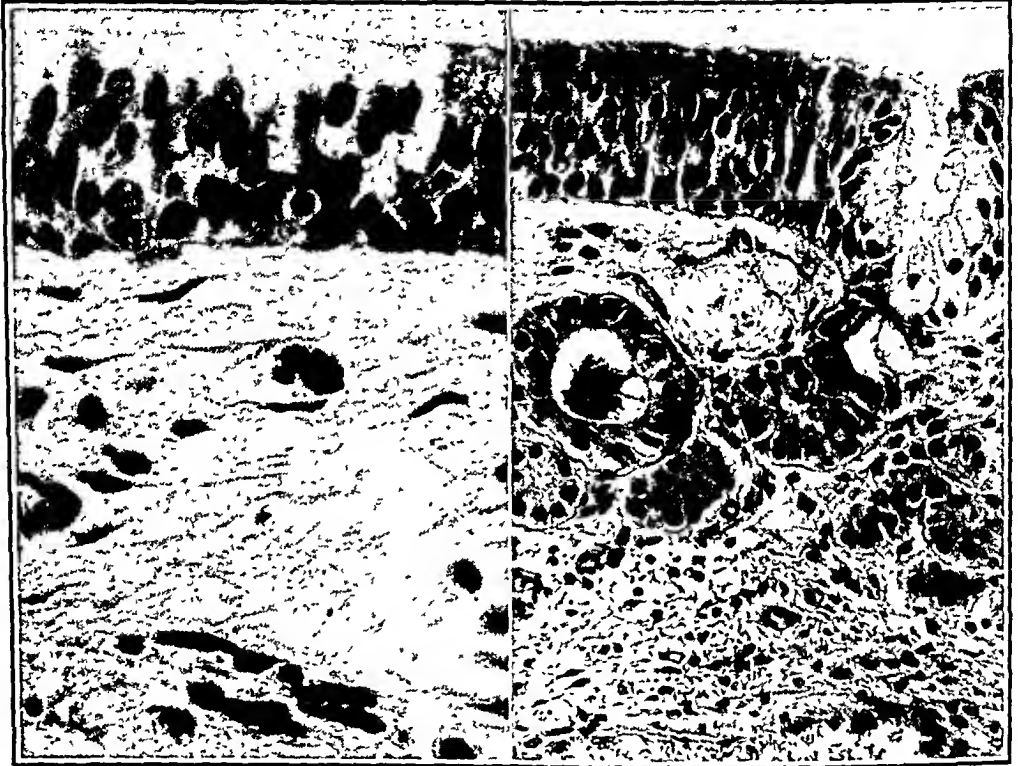


FIG. 85.

FIG. 86.

FIG 85 —Normal pseudostratified ciliated columnar epithelium from a maxillary sinus resting upon a distinct basement membrane. The tunica propria is composed of connective tissue and contains several capillaries x 400.

FIG 86.—Normal pseudostratified ciliated columnar epithelium from the nose resting upon a thickened basement membrane. The tunica propria contains several glands one of which opens onto the surface. x 200.

while the posterior ones open into the superior meatus. The *sphenoid sinus*, situated in the sphenoid bone and measuring 2x2x1.8 cm., opens into the spheno-ethmoidal recess which is located above the superior concha. The *maxillary sinus*, situated in the maxillary bone and measuring 3.5x3.2x2.5 cm., also opens into the middle meatus at a level inferior to that of the frontal and anterior and middle ethmoid cells. The ostium of the maxillary sinus and, to a lesser degree, that of the sphenoid sinus is above the level of the most dependent portion of the sinus whereas the orifices of other sinuses are below the levels of the cavities. The medial wall and floor are more or less flat and harbor no important structures.

Inflammation—Inflammation of the nose is known as rhinitis and inflammation of the sinuses is called sinusitis. Because of the close embryologic, anatomic and histologic relationship of these structures it is not surprising that an inflammatory disease of one organ is frequently associated with a similar process in the other. The two will, therefore, be considered together.

Non-Specific Inflammation—Acute Rhinitis and Sinusitis—The former is also known as the common cold, a cold in the head, acute coryza and catarrh and is often accompanied or followed by the latter. It is by far the most common disease affecting man and accounts for the loss of millions of man hours of labor annually. There are at least three factors that bring about a cold, namely, a virus, bacteria and a breakdown of body defenses. There is no longer any doubt that the initiating agent is a *filtrable virus* which can be cultivated on artificial media and which can also be successfully transmitted to man, chimpanzees and ferrets. It is, however, short lived and is responsible for only the first two days of the disease. Prolongation of the inflammatory process beyond this time is due to *secondary invasion by bacteria* which normally are



FIG. 89—Acute sinusitis. The surface is covered with a stream of mucus that is issuing from goblet cells. The tunica propria is edematous, infiltrated with neutrophils and contains active glands. $\times 75$

found in the nose and sinuses. Chief among these are streptococcus, pneumococcus, staphylococcus and influenza bacillus. *Natural defenses* consist of mucociliary activity, nasal ventilation and the ability of the body to adjust itself to sudden alterations in temperature. Normally cilia are in constant motion carrying mucus, bacteria and other particles towards the nasopharynx. They are, however, delicate structures and can perform optimum function only in the presence of (1) an adequate supply of moisture which is derived from goblet cells, submucosal glands and the atmosphere, (2) a pH range from 6.6 to 7.4, (3) neither too warm nor too cold

down around the protrusion, thus allowing its connection with the brain. *Grossly*, the lesion appears as a soft polypoid mass that protrudes into the posterior portion of the nasal cavity. It may pulsate with respiratory and circulatory oscillations and compression of the internal jugular vein may increase its firmness. Frequently,



FIG. 87.—Dermoid cyst from the root of a nose showing a lining of keratinized squamous epithelium and hair follicles and sebaceous glands in the wall x 50

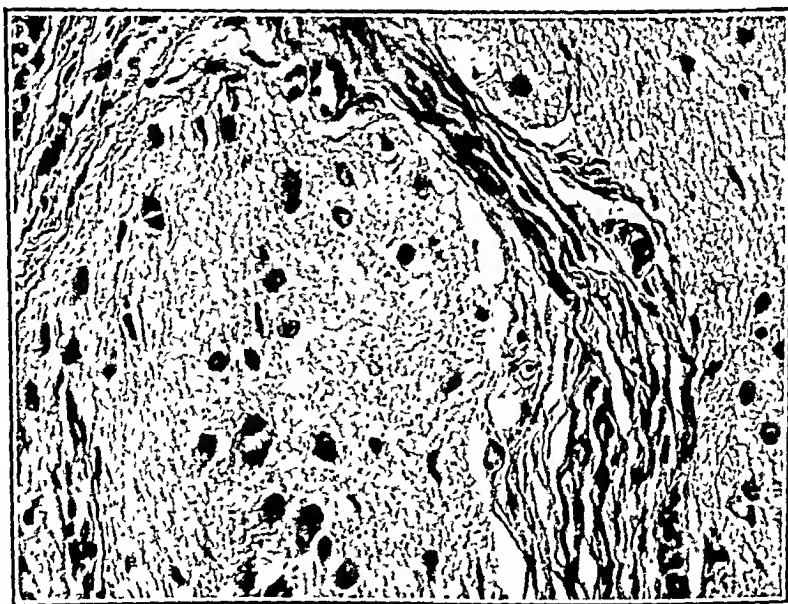


FIG. 88.—Encephalomeningocoele from the root of the nose showing brain tissue separated by strands of fibrous tissue x 200.

there is an escape of spinal fluid through the nose. *Histologic* sections reveal islands of brain tissue supported by fibrous septa (Fig. 88). In the past removal has often been followed by purulent meningitis but with the advent of chemotherapy the outlook is immeasurably improved.

even grey. Its surface is dull and dry or glistening and moist. It varies in thickness from 1 mm. to almost a centimeter depending upon the amount of accumulated edema fluid. The earliest *histologic* changes consist of an intense congestion of the submucosal capillaries followed by an exudation of serum, fibrin, neutrophils and, after the first twelve hours, of plasma cells and lymphocytes (Fig 89). Consequently, the stroma becomes edematous and greatly thickened. At about the same time the goblet cells of the surface epithelium and the submucosal glands are stimulated to maximum activity and pour their secretion on to the surface (Fig 90), cilia are destroyed, and many columnar cells are sloughed. As the infection subsides the fluid is resorbed, the inflammatory cells first become more numerous and then disintegrate or wander back into the capillaries, the surface epithelium regenerates and, except for residual fibrosis, the mucosa is usually restored to normal.

Chronic Non-Specific Rhinitis and Sinusitis — Chronic inflammation of the nose and sinuses results from a continuation of an acute

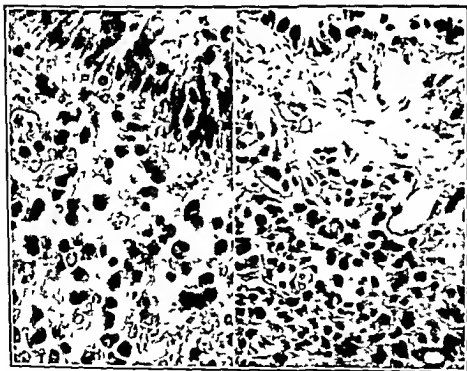


FIG 91

FIG 92

FIG 91 — Chronic non specific rhinitis. The epithelium is atrophic, partially ulcerated and its cilia are absent. The tunica propria is infiltrated with plasma cells. $\times 400$

FIG 92 — Allergic sinusitis. The epithelium is destroyed, the basement membrane is hyalinized and greatly thickened and the tunica propria is infiltrated with a variety of cells among which are eosinophils. $\times 200$

infection and is an expression of unusually virulent organisms, of poor "resistance" on the part of the patient and of improper treatment. The *symptoms* are the same as in acute inflammation with

atmospheric temperature and (4) proper nasal ventilation. The latter is extremely important for the inspiratory current of air cleanses the nose and sinuses by carrying with it bacteria loaded mucus into the nasopharynx. In the presence of obstruction ventilation ceases, mucus accumulates, cilia are injured, the mucosal barrier is lifted and the way is paved for infection. Failure of the body to adjust itself to sudden changes in temperature has a similar effect. It has been shown that exposure to cold produces a drop in nasal temperature and transient ischemia of the mucosa. Normally, a readjustment occurs almost immediately, but in the presence of physical fatigue, loss of sleep, constant worry or fear, ischemia may persist for hours. This results in diminution of secretions, a dry membrane, paralysis of the cilia, loss of local resistance and infection. The *symptoms* of acute rhinitis are sneezing, dryness and burning of the nose and pharynx, and chilliness, followed by malaise, headache,



FIG. 90.—Acute sinusitis showing maximum goblet cell activity. $\times 400$.

sore throat, cough, fever, abundant secretion and blocking of the airway. When the sinuses become involved there are in addition pain over the affected sinus and a nasal voice. The mucosa at first appears fiery red and dry, but later it becomes dull and covered with secretion.

The only opportunity that a pathologist has of examining an acutely inflamed nasal and sinusal mucosa is at necropsy for surgeons do not operate upon patients with acute coryza. At autopsy the process is as a rule widespread involving all cavities with almost equal severity. The *mucosa* is an intense fiery red to dull pink or

even grey. Its surface is dull and dry or glistening and moist. It varies in thickness from 1 mm. to almost 2 centimeter depending upon the amount of accumulated edema fluid. The earliest *histologic* changes consist of an intense congestion of the submucosal capillaries followed by an exudation of serum, fibrin, neutrophils and, after the first twelve hours, of plasma cells and lymphocytes (Fig 89). Consequently, the stroma becomes edematous and greatly thickened. At about the same time the goblet cells of the surface epithelium and the submucosal glands are stimulated to maximum activity and pour their secretion on to the surface (Fig 90), cilia are destroyed, and many columnar cells are sloughed. As the infection subsides the fluid is resorbed, the inflammatory cells first become more numerous and then disintegrate or wander back into the capillaries, the surface epithelium regenerates and, except for residual fibrosis, the mucosa is usually restored to normal.

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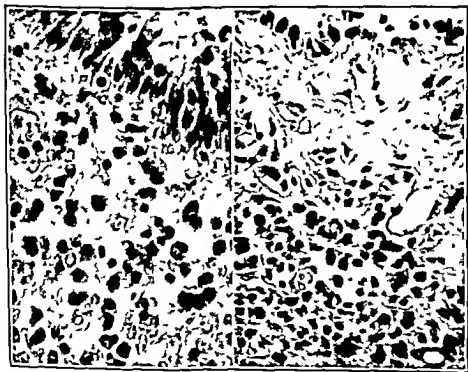


FIG 91

FIG 92

FIG 91—Chronic non specific rhinitis. The epithelium is atrophic partially ulcerated and its cilia are absent. The tunica propria is infiltrated with plasma cells. $\times 400$

FIG 92—Allergic sinusitis. The epithelium is destroyed the basement membrane is hyalinized and greatly thickened and the tunica propria is infiltrated with a variety of cells among which are eosinophils. $\times 200$

infection and is an expression of unusually virulent organisms, of poor "resistance" on the part of the patient and of improper treatment. The *symptoms* are the same as in acute inflammation with

emphasis upon post nasal drip, cough, blocked airway, pain and headache.

Grossly, the membrane is usually thicker than normal and sometimes it is definitely polypoid. It is grey or mottled grey, pink and hemorrhagic and the surface is dull. If edema is prominent the consistency is soft, but if it is in abeyance the mucosa is tough and fibrous. Often it becomes densely adherent to the underlying bone. The *histologic* changes are diffuse or focal. The epithelium is usually intact and often shows only a loss of cilia but sometimes it reveals patches of superficial or complete ulceration (Fig. 91). In the process of reparation it is restored to normal, becomes hyperplastic and even papillary, or it undergoes metaplasia to a stratified squamous type. The basement membrane becomes thicker and more prominent than it is normally but it does not attain the prominence seen in allergic inflammations. In the tunica propria the edema, that is so characteristic of the acute stage, gradually becomes replaced with a granulation tissue of fibroblasts, capillaries, plasma cells, lymphocytes and monocytic cells. In about 10 per cent of all purulent cases focal accumulations of leukocytic cells with destruction of underlying tissue eventuate in the formation of multiple microscopic abscesses. Submucosal glands are completely destroyed, become hyperplastic or, following an occlusion of their ducts, they become cystically dilated. The latter may attain a size of several centimeters in diameter. They are true cysts lined with flattened epithelium and are to be differentiated from pseudocysts which form as a result of an accumulation of edema fluid in connective tissue. Both are common and are found with equal frequency. *Resolution* occurs as in any other inflammatory process and it is deemed successful when the contiguity of the epithelium is restored, when the exudate is resorbed, when the glands regenerate and when the tunica propria is left with a minimum of fibrosis.

Allergic Rhinitis and Sinusitis.—The incidence of allergic inflammation of the nose and sinuses varies according to the season and the locality although generally speaking it is said that about one quarter of all cases of nasal and sinusal disease is on an allergic basis. The *allergens* likewise are variable but, if one discounts pollens that are prevalent only at certain times of the year, the most common offenders are house dust, feathers, orris root and bacteria. When an antigen comes in contact with a sensitized nasal or sinusal mucosa it is fixed by the endothelial cells of the capillaries. The consequent injury results in dilatation, hyperemia, and increased permeability of the vessel walls with exudation of fluid and leukocytes into the surrounding tissue or, in other words, an allergic inflammation. The *symptoms* are not distinctive and consist of sneezing, profuse discharge, blockage of the airway, cough and a nasal voice.

Grossly, this type of inflammation does not differ greatly from some hypertrophic types of non-allergic bacterial origin. The mucosa is many times the normal thickness. It is grey or bluish, boggy, edematous and in about one third of the cases it is associated with polyps. These are particularly prone to develop where the

vessels are numerous and the connective tissue is loose. In decreasing order of frequency they occur in the ethmoid, maxillary, frontal and sphenoid sinuses and around the ostia. The microscopic changes are quite characteristic although sometimes the picture is complicated by a superimposed bacterial infection. The epithelium is hyperplastic, often infolded and polypoid, discloses an increase in basal cells, and reveals a marked goblet cell activity. Sometimes, however, it is atrophic (Fig 92). The cilia are frequently desquamated and the basement membrane is hyalinized, greatly thickened and conspicuous. The immediately subjacent stroma discloses edema and when this is severe it eventuates in a prolapse of the mucosa and the formation of polyps. Throughout the tunica propria there is an infiltration with eosinophils, lymphocytes, plasma cells and fewer numbers of neutrophils. Eosinophils are particularly prominent about the superficial capillaries and the submucosal glands.

The diagnosis of rhinitis and sinusitis is ordinarily not difficult and the patient will frequently have a clear-cut understanding of his ailment before consulting a physician. From a therapeutic point of view it is important to differentiate between an allergic and a non-allergic infection. In the former a careful history may establish a seasonal occurrence and even reveal the offending allergen. The allergen can be further identified by skin tests. Also in allergic infections there is almost always an increase of eosinophils in smears of nasal and sinusal secretions. Roentgenograms of the sinuses will show an opacity in the presence of any extensive infection and this aid in diagnosis is, therefore, of great value in equivocal cases. Treatment of rhinitis and sinusitis is not standardized. In general one should endeavor to keep the airway open and to avoid anything, and particularly drugs, that will in any way injure the action of cilia. Frequently conservative measures will suffice but sometimes surgical interference in the form of removing polyps, correcting deformities and enlarging or making new ostia is necessary. In allergic states, however, surgical treatment is of no permanent value unless it is supplemented by appropriate anti-allergic therapy. The complications of sinusitis are many and may be listed as orbital cellulitis, osteomyelitis, meningitis, brain abscess, possibly bronchiectases, arthritis, otitis media, mastoiditis, cavernous sinus thrombosis, abscess of the nasal septum, sinusal empyema (loculated pus due to a closed or stenotic ostium) and mucocele (collection of mucus in a sinus often resulting from a closed ostium in the presence of a low grade infection). The prognosis with regards to mortality is excellent but with regards to morbidity it is poor.

Atrophic Rhinitis—This affliction has also been called *ozena*, atrophic catarrh, *coryza foetida*, sclerotic rhinitis and, less elegantly but nevertheless befittingly, *plain stink nose*. It is a chronic disease of the nasal cavity characterized by atrophy and crusting of the mucosa and accompanied by an offensive odor. It usually starts before twelve years of age and affects females five times as frequently as it affects males. While some authors divide the disease into two types, namely, primary and secondary to an apparent chronic

inflammation, it is more logical to consider the former as merely the end stage of the latter. The *cause* of the inflammatory and atrophic process is, however, an enigma. Among others the following have at one time or another been considered as of etiologic importance: heredity, specific ferment, a form of syphilis or tuberculosis, a wide nose and external nares, osteomalacia or osteitis of the ethmoid inferior turbinate and other bones, cholesterol unbalance, avitaminosis, endocrine disorder, chronic infection caused by bacillus foetidus ozaenae, and chronic nonspecific rhinitis and sinusitis associated with atrophic changes in the mucosa. The latter seems to be the simplest and most plausible explanation for if patients are seen early and followed over a period of many years all degrees from ordinary chronic rhinitis to the final atrophic stage are noted and furthermore if they are treated while in the former state the disease may be aborted. The dividing line between reversible and irreversible mucosal changes depends upon the state of the arteries. When they are unobstructed the disease is that of ordinary chronic rhinitis but when their lumens become occluded there develops an ischemic atrophy of the mucosa with all the consequent permanent secondary changes or, in other words, atrophic rhinitis. *Symptoms* consist of an offensive odor from the nose which in women is worse during the menstrual period, of a thick crusted nasal discharge, of obstruction to breathing and of a dry nose and throat. Examination discloses wide external nares, roomy nasal chambers, some mucopurulent secretion and a mucosa covered with yellowish green, brown or black crusts.

Grossly, the mucous membrane is atrophic. In early cases the *histologic* changes do not differ from those in ordinary chronic rhinitis. The cilia are clumped and in patchy areas completely absent; columnar cells disappear, and there is focal metaplasia to a stratified squamous type of epithelium. The basement membrane is thinner than normal but the submucosal glands are essentially unchanged. Scattered throughout the tunica propria there is an increase in lymphoid cells and to a lesser degree in plasma cells and only a moderate increase in fibrous tissue. Newly formed vessels are still apparent. There is little perivascular increase of fibrous tissue and the arteries do not show fibrosis of their walls or occlusion of their lumens. In the advanced stage the epithelial changes, although still patchy, are nevertheless more pronounced so that there is more and more of the abnormal stratified squamous cell type of epithelium and less and less of the normal pseudostratified columnar type. The basement membrane disappears. The tunica propria is massively and diffusely replaced with dense sclerotic acellular fibrous tissue which, as it contracts, chokes off both the ducts of the submucosal glands and the arterial supply. Consequently the glands disappear and those that remain tend to become cystically dilated. In addition to the perivascular fibrosis, the media and intima of the arterial wall become thickened and fibrotic. This eventuates in an occlusion of the lumen and an ischemia of the mucosa already referred to. The degenerative and fibrotic processes extend to the underlying bones and nerves resulting in an absorp-

tion of the former and, with destruction of the latter, of complete anosmia to the patient.

In the early stage the disease is, of course, indistinguishable from ordinary rhinitis. In the advanced stage the wide external nares, the bilateral nature, the roomy nasal cavities, the peculiar odor, and the extensive crusting are quite characteristic. Confusion with a foreign body, rhinolith or syphilis can be avoided if it is remembered that these diseases are as a rule unilateral. In early stages *treatment* is similar to that in any chronic rhinitis and is frequently quite satisfactory. In the advanced stages of the disease one cannot hope for a cure because the fibrotic and vascular changes are irreversible. *Treatment*, therefore, should be symptomatic and directed towards keeping the nose clean and free of crusts.

Specific Inflammation—Tuberculosis—Tuberculosis of the nose is not common despite the fact that tubercle bacilli are often found in nasal secretions and upon the mucosa. The disease usually attacks undernourished and anemic persons, starts in the first two decades of life, affects females three times as often as males, is frequently characterized by remissions and exacerbation, and is slowly progressive over a period of many years. The causative organism is the tubercle bacillus of both the human and bovine strains. Early *symptoms* consist of a nasal discharge. Later there are crusting, fetor and obstruction to breathing. The *site of predilection* is the mucosa covering the cartilaginous portion of the nasal septum whence it spreads to the floor and the anterior part of the inferior turbinate. The disease is usually bilateral. *Grossly*, the initial lesions exist as tiny discrete pink granules that extend peripherally and ulcerate centrally. The surface is covered with a sticky secretion which upon drying results in the formation of scabs. Sometimes the lesion exists as tumors that measure as much as 2 cm. in diameter. These also break down and ulcerate both onto the surface and through the septum leaving an irregular perforation. Healing by fibrous tissue is accompanied by contraction so that in old, chronic cases the tip of the nose is often pulled down towards the upper lip.

Histologically, the characteristic structure is the tubercle composed of epithelioid cells, Langhans' giant cells, plasma cells and lymphocytes. Caseation necrosis is not marked but intense secondary infection often masks the nature of the primary lesion. The *diagnosis* depends upon isolation of tubercle bacilli and the histologic appearance of tissue removed surgically. *Treatment* consists of destruction of the involved area with cautery or complete excision. The *prognosis* in early cases is fair but in advanced cases it must always be guarded. *Complications* consist of an extension of the disease to the lower portions of the respiratory tract, to the face, to the eye by way of the lacrimal duct and to the maxillary sinus.

Tuberculosis of the *sinuses* is less frequent than that of the nose. The maxillary antrum is the most commonly affected and the disease gains entrance by direct extension from the nose, from the teeth or from the eye and by blood stream metastases from a distinct focus elsewhere in the body. *Symptoms*, if any, are those of chronic sinusitis. Early in its course the *mucosa* is pale, boggy and often

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Specific Inflammation—Tuberculosis—Tuberculosis of the nose is not common despite the fact that tubercle bacilli are often found in nasal secretions and upon the mucosa. The disease usually attacks undernourished and anemic persons, starts in the first two decades of life, affects females three times as often as males, is frequently characterized by remissions and exacerbation, and is slowly progressive over a period of many years. The causative organism is the tubercle bacillus of both the human and bovine strains. Early *symptoms* consist of a nasal discharge. Later there are crusting, odor and obstruction to breathing. The *site of predilection* is the mucosa covering the cartilaginous portion of the nasal septum whence it spreads to the floor and the anterior part of the inferior turbinate. The disease is usually bilateral. *Grossly*, the initial lesions exist as tiny discrete pink granules that extend peripherally and ulcerate centrally. The surface is covered with a sticky secretion which upon drying results in the formation of scabs. Sometimes the lesion exists as tumors that measure as much as 2 cm. in diameter. These also break down and ulcerate both onto the surface and through the septum leaving an irregular perforation. Healing by fibrous tissue is accompanied by contraction so that in old, chronic cases the tip of the nose is often pulled down towards the upper lip.

Histologically, the characteristic structure is the tubercle composed of epithelioid cells, Langhans' giant cells, plasma cells and lymphocytes. Caseation necrosis is not marked but intense secondary infection often masks the nature of the primary lesion. The *diagnosis* depends upon isolation of tubercle bacilli and the histologic appearance of tissue removed surgically. *Treatment* consists of destruction of the involved area with cautery or complete excision. The *prognosis* in early cases is fair but in advanced cases it must always be guarded. *Complications* consist of an extension of the disease to the lower portions of the respiratory tract, to the face, to the eye by way of the lacrimal duct and to the maxillary sinus.

Tuberculosis of the sinuses is less frequent than that of the nose. The maxillary antrum is the most commonly affected and the disease gains entrance by direct extension from the nose, from the teeth or from the eye and by blood stream metastases from a distinct focus elsewhere in the body. *Symptoms*, if any, are those of chronic sinusitis. Early in its course the *mucosa* is pale, boggy and often

polypoid but later it becomes caseous, ulcerates and sloughs, filling the sinus cavity with pus and necrotic tissue. With progress of the disease the underlying bones become affected and fistulous tracts are formed between the sinuses and adjacent structures. The *histologic* structure is similar to that found in the nose and elsewhere (Fig. 93). As in the nasal cavity the *diagnosis* is made by isolating tubercle bacilli and by biopsy. *Treatment*, consisting of radical resection, can only be carried out on early lesions. Usually, however, the local disease is too far advanced to permit such a measure. The *prognosis* is poor not only because the infection in

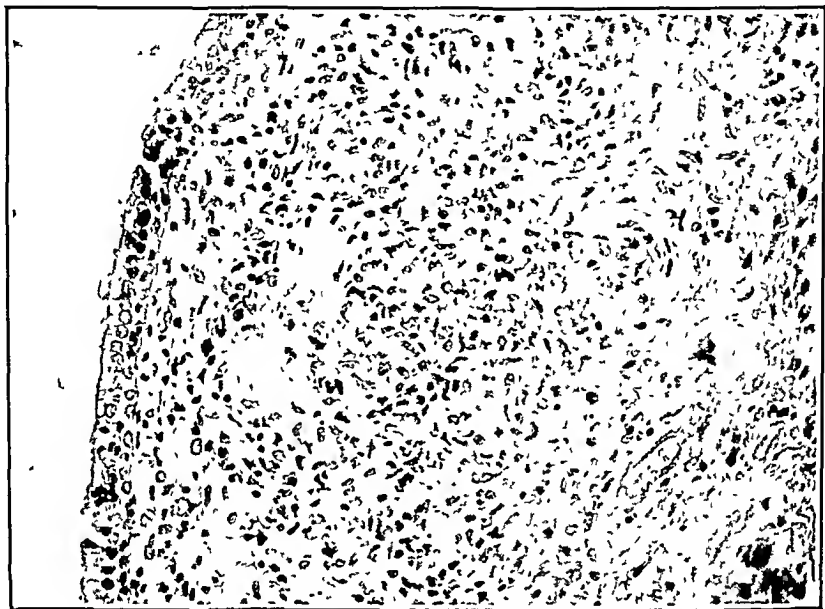


FIG 93 —Tuberculous sinusitis. The tunica propria contains several tubercles composed solely of epithelioid cells. There are no giant cells. x 100

the sinus cannot be eradicated but because there is often an associated, advanced, pulmonary tuberculosis.

Sarcoid.—Boeck's sarcoid of the nose is not a common disease. It may occur as part of a more severe systemic involvement or it may be the only active focus in the body. An annoying nasal discharge is the most constant *symptom*. The *lesions* usually occur on the turbinates or on the septum as small tubercles that gradually coalesce to form pearly white granular masses. Progressive atrophy and crusting of the turbinates has been noted and perforation of the septum has been described. The *histologic* changes are similar to those already described in the skin. The most satisfactory *treatment* is surgical excision. *Recurrences* are frequent.

Syphilis.—As in the skin syphilis of the nose may be divided into primary, secondary and tertiary varieties.

Primary syphilis of the nasal cavity is rare and is always of the acquired type. The mode of infection is contact with contaminated articles aided perhaps by picking at the nose with the finger. A chancre usually appears in the vestibule or in the anterior part of the septum in from three to four weeks after inoculation. It is a raised, hard sore with a deeply ulcerated surface from which

oozes a slight discharge. Healing is spontaneous in from six to ten weeks leaving little or no scarring.

Secondary syphilis of the nose is rarely required but is frequently congenital. Although symptoms are often present at birth they may not be manifest until three or four months later. Characteristically, they consist of a nasal catarrh commonly called snuffles. The nose is filled with first a thin and then a thick yellow secretion that soon dries and forms crusts. Externally, radiating from the alae nasi, there are deep moist fissures and ulcers, and elsewhere over the body there are other manifestations of secondary syphilis.

Tertiary syphilis of the nose occurs both in the acquired and hereditary form. In each the disease becomes manifest soon after the secondary stage or at any time thereafter. The characteristic lesion is the *gumma* and it may affect the septum, inferior turbinate, floor, vestibule or the alae nasi. There are no early symptoms but later there are nasal obstruction, pain, discharge, crusting and anosmia. As elsewhere the gumma varies in size, is elastic and soon breaks down and ulcerates. The ulcer is irregular in outline, the margins are thick indurated and overhanging, and the excavation penetrates to the underlying bone and cartilage. Soon even the latter are involved and destroyed, resulting in the sequestration of osseous and cartilaginous tissue and eventuating in perforations of the septum, hard palate and maxillary, sphenoid and ethmoid bones. Healing is by fibrous tissue formation. When the septum is destroyed contraction of scar tissue produces retraction of the root of the nose and the characteristic "saddle" deformity.

The *histopathologic* changes in primary, secondary and tertiary syphilis of the nose are identical to those in the skin and since these were considered in detail in Chapter I they need not be re-described here. The *diagnosis* is greatly facilitated by finding stigmata of the disease in other organs and tissues. A positive blood Wassermann is always of value. In fungating lesions, however, the similarity to malignant tumors is often striking and a differentiation can be made with certainty only by resorting to biopsy. *Treatment* consists of local hygiene measures and anti-syphilitic therapy. The *prognosis* in other than the primary stage must be guarded for infants with secondary congenital syphilis are often weak and die from inanition, and patients with tertiary lesions develop severe nasal deformities or they may die from meningitis.

Glanders—Glanders is an infectious disease of the nasal cavity of animals, particularly horses, that is sometimes transmitted to grooms, farmers and others who are associated with these quadrupeds. *Bacillus mallei* is the causative organism. It is a slender, somewhat beaded, non-motile, gram negative rod that is found in nasal secretions and discharges from infected animals and man. It gains entrance to the nose by inhalation or by digital transfer of infected material. The incubation period is three to six days but the organism may remain dormant for many months before it produces the disease. Initial *symptoms* consist of fever, malaise, pains in the limbs and prostration and are soon followed by a profuse, yellowish brown or sanguineous, fetid nasal discharge.

The *lesions* appear in the nasal mucosa as small nodules that rapidly liquefy, discharge onto the surface, and produce irregular ulcers with grey bases and undermined edges. The disease spreads by contiguity to the adjacent mucosa and underlying bone and by lymphatic vessels to the draining lymph nodes. Ultimately, in the more chronic cases, there is complete destruction of the nasal septum, turbinates, sinuses, soft palate and even the laryngeal cartilages. *Histologically*, the lesion is a specific granuloma the structure of which varies somewhat according to the age of the disease. Initially there is a central focus of complete necrosis composed entirely of detritus and nuclear fragments (Fig. 94). Disposed about the

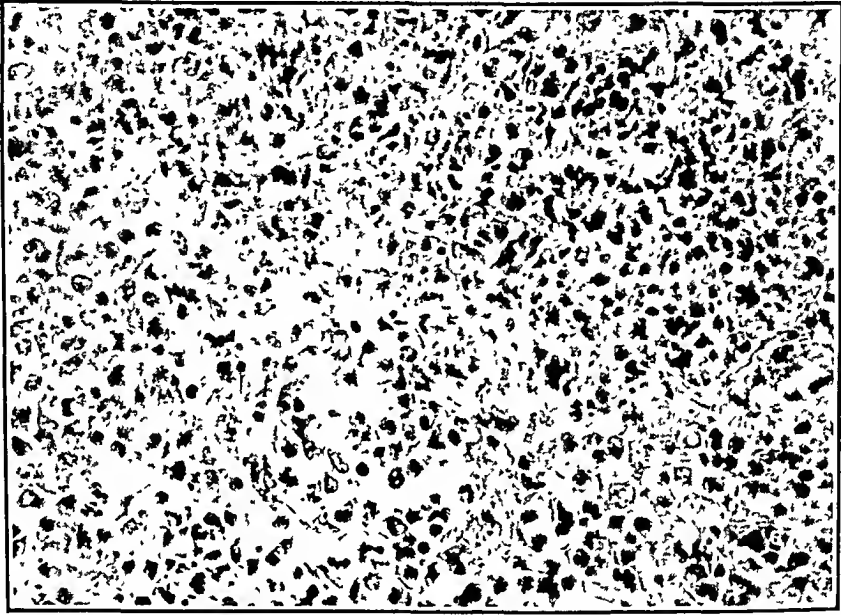


FIG 94.—Glanders. In the upper right hand corner, there are nuclear fragments and neutrophils. At the periphery, there are neutrophils, epithelioid cells, plasma cells and fibrin threads. $\times 200$.

periphery there are neutrophils, fewer lymphocytes and fibrin threads, and between these collections there is a stroma of loose connective tissue, capillaries, neutrophils, lymphocytes, plasma cells and extravasated erythrocytes. Gradually, epithelioid cells are added either between the necrotic and neutrophilic zones or beyond the latter; giant cells of the Langhans' or foreign body type may be seen here and there; endothelial cells lining the vessels become hyperplastic, and fibrosis becomes apparent.

The *diagnosis* of glanders is suspected when an abruptly appearing nasal lesion is preceded by generalized toxic symptoms in a person who has had contact with horses. It is confirmed by cutaneous sensitivity tests, agglutination, precipitin or complement fixation reactions performed on the patients serum, or by isolating the bacillus mallei. The latter can be best accomplished by inoculating the peritoneal cavity of a male guinea pig with discharges from a lesion. If organisms are present the animal will develop an inflammation of the spermatic cord and tunica vaginales in from

twenty-four to forty-eight hours and cultures of this on a potato will yield a growth of *bacillus mallei*. *Treatment* is unsatisfactory and consists chiefly of local symptomatic therapy. A vaccine has been tried but is of questionable value. The *prognosis* is grave for most patients die in from one week to four months although in chronic cases the disease may last as long as fifteen years.

Leprosy—Leprosy of the nasal cavity is common among lepers for it is said (without definite proof) that this is the route of invasion of the bacilli. The disease is insidious and frequently *symptoms* do not develop for ten years or more after exposure. Early there may be a nasal discharge and epistaxis whereas in cases where the disease is advanced there are a nasal voice, hoarseness and dyspnea. *Pathologically*, the lesions are essentially the same as they are in the skin except that the nodular form is the rule and the maculo-anesthetic type the exception. Sometimes the two varieties are combined. The disease starts in the septum and the turbinates is a diffuse reddish thickening of the mucosa. Later, the lesions become pale anemic and nodular. These coalesce, break down, ulcerate, discharge muco-purulent material and become crusted. The septum and turbinates are destroyed and with the formation of cicatricial adhesions the apex of the nose may be retracted. The disease *spreads* to the posterior nares, palate, oral fauces, tonsils, pharynx, larynx, tongue and gums everywhere producing nodular, ulcerating, cicatricial, deforming lesions. In the skin of the face it forms heavy furrowed infiltrations over the orbits, nose, lips and chin which result in what has aptly been called a lion-like facies. The *histologic* changes are identical with those in the skin. The disease may be confused with tuberculosis and syphilis. The *diagnosis* is made by finding stigmata of the disease elsewhere, by demonstrating the bacilli of leprosy in nasal discharges and by biopsy. *Treatment* is non-specific and is directed towards keeping the nasal cavity free of discharges and crusts. The *course* is protracted and the ultimate *prognosis* is poor.

Scleroma—This disease was first considered as a "granulation sarcoma," was later called rhinoscleroma, and more recently it has been named simply scleroma. It is a slightly infectious, chronic granulomatous disorder that usually originates in the nasal cavity, whence it spreads to the upper lip, cheeks, antrum, lacrimal ducts, pharynx, eustachian tubes, gums, palate, tonsils, larynx, trachea and even bronchi. At one time it was thought that the disease was limited to central and southeastern Europe, but now it is known that no part of the world is immune. Over 100 cases have been reported from Canada and the United States. It is a disease of the lower stratum of life, first becomes manifest between sixteen and thirty-five years of age, and attacks three women to every two men. The causative organism is considered by some to be the *bacillus rhinoscleromatis* or the von Frisch bacillus—a gram negative, encapsulated rod that is readily cultured from the lesions of all cases of scleroma. Since this organism is also found in nasal secretions from healthy persons, some authors do not consider it as the etiological agent and prefer to incriminate a virus which as yet has not been isolated.

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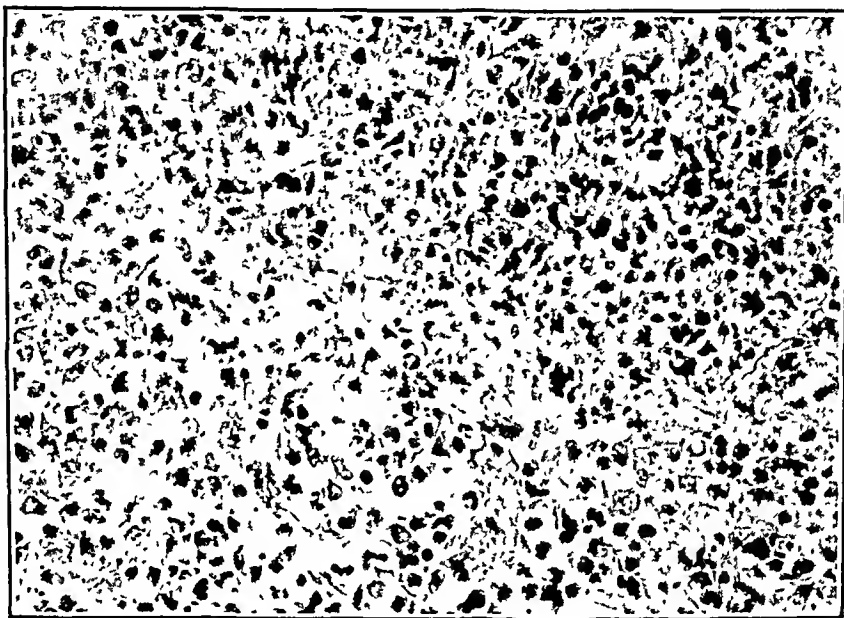


FIG 94.—Glanders. In the upper right hand corner, there are nuclear fragments and neutrophils. At the periphery, there are neutrophils, epithelioid cells, plasma cells and fibrin threads. x 200.

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or vacuolated and light staining, and their nuclei are small, round, oval, evenly stained and centrally or eccentrically placed. They contain the bacillus rhinoscleromatis and are quite characteristic although they are not necessarily pathognomonic. As the lesion becomes older, neutrophils and Mikulicz cells are replaced by plasma cells and Russell's bodies (Fig. 96). The origin of the latter is still in dispute but it is probable that they arise from plasma cells. They are round or oval, at first ill-defined and then sharp, intensely eosinophilic masses that measure from 10 to 40 microns in diameter. The younger bodies have nuclei that are similar to those of plasma cells but as they become older the nuclei become pyknotic, irregular, broken up and finally they disappear. With increasing age connective tissue becomes more and more abundant and fibrous and all inflammatory cells become less and less conspicuous.

A correct diagnosis can be established only by culturing the causative organism and by removing a piece of tissue for histologic study. Of importance microscopically are Mikulicz cells and Russell's bodies. Treatment is unsatisfactory. Although most medicines have been tried there is none that is of permanent value. The best results have been obtained by surgical excision, electrocoagulation or irradiation. The ultimate prognosis is poor for the disease is slowly but steadily progressive usually over a period of several decades. Death results from intercurrent infection or asphyxia.

Rhinosporidiosis—This is a fungus infection caused by *rhinosporidium secheri* that ordinarily affects the nose but has also been described as a primary lesion of the pharynx, uvula, conjunctiva and skin. It is found in all parts of the world, usually starts before the age of thirty years and affects 3 males to every female. The source of infection is not known but it is thought by some that the organism is water borne. Although the disease has been described in horses and cows it has never been transmitted to experimental animals. In man symptoms are of a few weeks to many years duration and consist of a thin or mucoid discharge, epistaxis and obstruction.

The characteristic gross lesion is a polyp. It is usually unilateral and single but it may be bilateral and multiple. Its point of origin is most frequently the anterior part of the nasal septum or the floor although it may also arise from the middle and inferior turbinates and the superior, middle or inferior meatus. The growth is pedunculated or sessile, distinctly papillomatous, pink or deep red, speckled with minute grey granules, soft and bleeds freely upon the slightest trauma. Histologically, the polyp is covered with a hyperplastic layer of stratified squamous epithelium. The stroma of fibrous connective tissue is dense centrally and loose and myxomatous peripherally. It contains numerous engorged thin walled capillaries, dense nodular infiltrations with plasma cells and lymphocytes, fewer numbers of neutrophils and eosinophils, occasional giant cells, foci of hemorrhage, blood pigment and most important of all—the rhinosporidia secheri. These are found within the stroma, intraepithelially and intermingled with the mucus that covers the polyp and fills the crypts between the papillae. Most if not all of

Symptoms are insidious. Early they consist of a foul nasal discharge and crusting of the mucosa, whereas later there are blockage of the airway, epistaxis and distortion of the nasal aperture. When the lesion has involved other organs there may also be hoarseness, a brassy cough, dyspnea, deafness, tinnitus and sinus headache.

Pathologically, the lesion may be diffuse and infiltrating or nodular in type. Initially, the former produces a thin dry mucosa that is covered with yellow crusts. Later it results in a thickened, hard, contracting, cartilaginous-like mass that penetrates deeply and eventuates in much distortion of the nasal cavity. The nodular variety originates as circumscribed, red to violet, edematous nodules that measure 2 to 3 mm. in diameter. Gradually they enlarge and coalesce resulting in tumefactions of varying sizes. As they grow older they too become distorted, their appearance changes first to light yellow and then to grey, and they become firm and sclerotic.

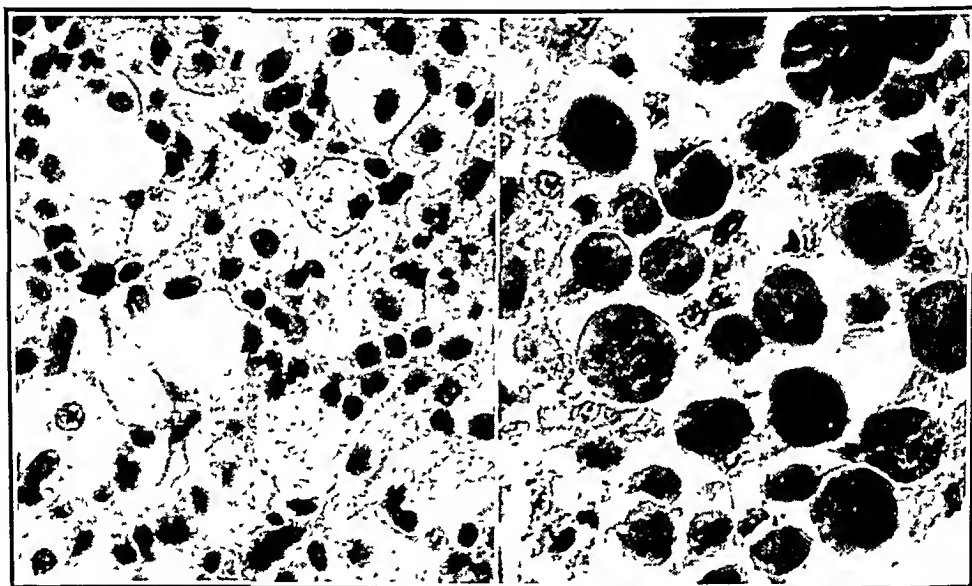


FIG 95

FIG 96.

FIG 95.—Scleroma showing numerous Mikulicz cells. x 400
FIG 96.—Scleroma disclosing numerous Russell's bodies x 400.

The *histologic* picture differs somewhat according to the age of the lesion. The epithelium may be intact or superficially ulcerated. It is usually of the stratified squamous cell type and may be thin and atrophic or greatly hyperplastic. The latter reveals little or no keratin and shows prominent prickle cells, inter-cellular bridges, and rete cones. Specific lesions are found in the tunica propria. The cellular infiltration is either diffuse and unrestrained or it is focal and surrounded by a capsule of compressed fibrous tissue. In early cases the stroma is scanty, vascular and composed of loose connective tissue. Dispersed uniformly throughout the tissue there are numerous neutrophils, fewer eosinophils and a varying number of *Mikulicz cells* (Fig. 95). These are large, round, oval or polygonal foam cells that measure from 100 to 200 microns in diameter. Their outlines are sharp; their cytoplasm is reticulated

that are considered in the chapter on bone, from dental structures a cyst, an odontoma and an adamantinoma, and from lymphoid tissue a lymphosarcoma. In addition to the aforementioned neoplasms the nose and sinuses are sometimes the seat of a metastatic cancer. Clinically the only three tumors that are frequent enough to justify a more detailed description are polyp, ossifying fibroma and carcinoma.

Polyp—Most polyps of the nose and paranasal sinuses are not true neoplasms and the only justification for including them under tumors is that they produce tumor-like formations. They have been considered to arise as a result of (1) a lymphatic vascular disease similar to that in elephantiasis, (2) a constitutional or hereditary disturbance and (3) an inflammatory process in the form of a diffuse non-specific infection, suppuration of the sinuses or an



FIG. 98.—Nasal polyp showing an irregularly congested external surface and a myxomatous cut surface.

allergic disorder. The latter is doubtlessly the greatest single cause of polyps accounting for at least two-thirds of all cases. The offending allergens are protean, and include not only dust, hair, feathers and pollens but also bacteria. Polyps are usually found between the ages of twenty and thirty years, affect men more frequently than women, are unilateral or bilateral and are usually multiple. Symptoms consist of slowly progressive nasal obstruction, nasal voice, persistent and sometimes copious watery discharge and headache.

In the nose polyps usually arise from the mucosa around the middle meatus or from that in the ethmoidal region. The most commonly involved sinuses are the maxillary and the ethmoid. Polyps originating in the former have a tendency to protrude through the ostium into the nasal cavity and even into the nasopharynx.

the stages of the developmental cycle through which the fungus passes can be found in a single specimen (Fig. 97). Initially the organism is round or oval, measures about 6 microns in diameter, and reveals a sharp chitinous membrane, a vacuolated cytoplasm and a vesicular nucleus. When a size of 60 microns is attained mitotic division of the nucleus commences. This continues until there are about 4000 nuclei at which time the cytoplasm also divides. Two subsequent divisions bring the total number of spores to 1600. These mature upon reaching a size of 6 microns and, with rupture of the wall of the sporangium, they are liberated to repeat the cycle.

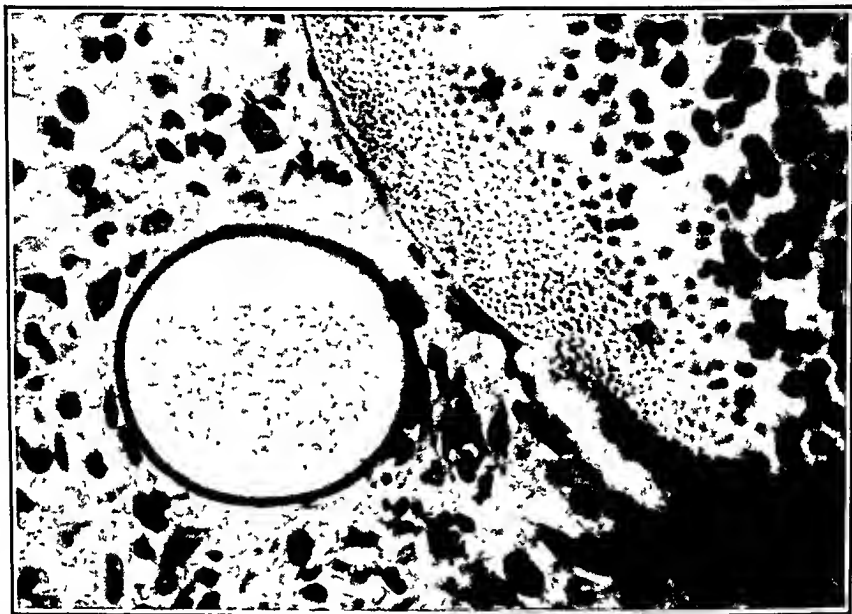


FIG 97.—Rhinosporidiosis illustrating the rhinosporidium in various stages of development x 400

Rhinosporidiosis should be suspected whenever a patient presents himself with a unilateral nasal polyp that bleeds readily upon manipulation. The *diagnosis* is confirmed by finding the causative organism in nasal discharges and in histologic sections of removed tissue. *Treatment* consists of excision of the polyp and the surrounding mucosa either surgically or by electric cautery. *Recurrences* are common.

Tumors.—Some tumefactions in the nose and paranasal sinuses are common whereas others are infrequent enough to be considered as curiosities. Almost all of the normally present tissues have been known to produce an innocent or a malignant tumor. Thus from the epithelium there develops a papilloma, Bowen's disease and a carcinoma; from submucosal glands a cyst, an adenoma (mixed tumor) and an adenocarcinoma; from connective tissue a polyp, a fibroma, an ossifying fibroma, a fibrosarcoma, a myxoma and a myxosarcoma; from fat tissue a lipoma; from blood vessels an angioma and an angiosarcoma; from lymph vessels a lymphangioma; from nervous elements a neurofibroma and a melanoblastoma; from cartilage a chondroma; from osseous tissues many of the tumors

numerous as to suggest an angioma or they may be in complete abeyance (Fig 101). The same is true of submucosal glands. In some polyps they are increased in number and size whereas in others there are none present. Sometimes the ducts become obstructed, mucus accumulates in the lumen, and the glands become cystically dilated. Usually, there is some degree of inflammatory cell infiltration but occasionally, it is so marked as to overshadow all other structures. In allergic conditions eosinophils predominate whereas in polyps of non-allergic origin plasma cells, lymphocytes, neutrophils and mononuclear phagocytes are more conspicuous.

A diagnosis of nasal polyps is easy if, when necessary, one takes the trouble to anesthetize the mucosa with cocaine and to examine the nose thoroughly. Of importance from a differential standpoint are deviation of the septum, deformed turbinates, malignant tumors



FIG 101—Nasal polyp showing atrophy of the epithelium and numerous vascular spaces in the underlying tissue, imparting an angiomatous appearance $\times 50$

and a meningocoele. Fewer mistakes will be made if, contrary to custom, all polyps that are removed surgically are subjected to histological examination. *Treatment* is twofold: (1) remove the tumor and (2) attend to the underlying or causative condition. The latter is of particular importance in allergic disorders. The *prognosis* must always be guarded for recurrences are common.

Ossifying Fibroma—As the name implies this tumor is primarily a fibroma containing osseous tissue. Some of the *synonyms* are osseous fibroma, fibro-osteoid osteoma, central osteoma, osteofibroma, sclerosing fibroma, hypertrophic localized osteitis, localized osteodystrophic fibroma, and localized osteitis fibrosa. The neoplasm ordinarily occurs in the maxilla and the mandible, is usually unilateral, is found before the age of thirty years in two-thirds of cases, and affects females more commonly than males. It grows slowly but progressively and when it erodes the bones it produces a

When small or few in number the *tumors* may be seen to lie free in the nasal cavity, but when they are large or multiple they block and distend the entire cavity. They may even cause separation of the nasal bones eventuating in an external deformity. Polyps vary in size from a few millimeters to 12 cm. or more (Fig. 98). The pedicle of the former is usually broad whereas that of the latter is narrow. The growths are dark red, pink or grey. They are soft, freely movable and do not bleed readily upon manipulation—a feature which helps to distinguish ordinary benign polyps from malignant tumors and from tumor-like formations caused by *rhinosporidium seeberi*. The external surface is frequently ulcerated



FIG 99

FIG. 100.

FIG 99 —Nasal polyp The epithelium is greatly hyperplastic and stratified squamous. The underlying tissue is dense, fibrous and acellular. x 50

FIG 100 —Nasal polyp. The epithelium is hyperplastic, pseudo-stratified ciliated columnar and the underlying tissue is myxomatous and infiltrated with inflammatory cells. It contains engorged capillaries and numerous hyperplastic glands x 50

and covered with a purulent exudate. Cut surfaces vary from solid grey, pink or hemorrhagic to myxomatous or frankly cystic. *Microscopically*, the epithelium is intact or superficially ulcerated. It is of a normal or a hyperplastic pseudostratified ciliated columnar type or it is greatly thickened and of a stratified squamous variety. The basement membrane may or may not be prominent. The stroma is composed of dense, acellular, hyalinized fibrous tissue or loose, edematous and myxomatous connective tissue (Figs. 99 and 100). Edema may at times be severe enough to completely destroy the latter and thereby to form false cysts. Vascular spaces in the form of thin walled capillaries or large cavernous sinuses may be so

Symptoms are similar in carcinoma of a *paranasal sinus* when the tumor has broken into the nasal cavity. Since the maxillary sinus is most frequently involved additional symptoms may consist of obstruction of the lacrimal duct, loosening of the upper teeth and bulging of the cheek and orbit. In the nose the tumor is located on the septum or high on the lateral wall, whereas in the sinuses the point of origin is difficult to determine because usually by the time a diagnosis is made the entire cavity is involved.

Grossly, the lesions tend to be polypoid. They are moderately firm, bleed easily upon manipulation and are as a rule superficially ulcerated and infected. *Histologically*, they may be divided into three types, (1) adenocarcinoma, (2) squamous cell carcinoma and (3) anaplastic carcinoma. *Adenocarcinoma* is uncommon and of a low grade malignancy. It arises from submucosal glands. It is probable that most tumors of this variety are not true adenocarcinoma, but are in reality adenomas with malignant potentialities.

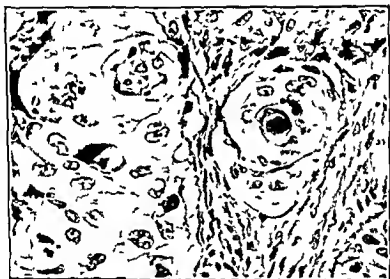


Fig. 103—Squamous cell carcinoma of the nose showing two masses of polyhedral neoplastic cells in one of which there is an epithelial pearl. $\times 200$

They are similar to one of the types of benign adenoma found in the trachea and bronchi. In stratified *squamous cell carcinoma* the surface epithelium may be intact or ulcerated. If sections are made at the correct level nests and cords of irregular epithelial cells are seen to stream from the basal layer into the underlying stroma. The cells vary in shape and size. Most are large, sharply defined and have an abundant amount of pale or eosinophilic cytoplasm (Fig. 103). The nuclei are large, round, oval or irregular. They are hyperchromatic or vesicular, frequently disclose nucleoli and are often in a state of mitosis. Pearl formation may be marked or scanty. The supporting stroma varies in amount, but is usually fibrous and is almost always infiltrated with plasma cells, lymphocytes, neutrophils, and mononuclear phagocytes. Occasionally the latter are distended with lipid material and when numerous

bulging of the cheek, the palate or the alveolar ridge. The teeth of the affected jaw may be healthy or carious and frequently a tooth may have been extracted because of a vague toothache.

Grossly, the tumor is grey with often a yellowish tinge, is not encapsulated, is firm and cuts with the resistance of a green pear. *Histologically*, the lesion exhibits interlacing bundles of loose or dense fibrous tissue (Fig. 102). The cytoplasm is abundant, eosinophilic and often fibrillated at the periphery of the cell. The nuclei are attenuated and spindle shaped or they are short, plump and evenly but deeply stained. Scattered throughout there are varying numbers of thin small spicules of eosinophilic osteoid tissue. Frequently the center is calcified and usually the periphery is surrounded by a single or double row of plump osteoblasts. Giant cells of the foreign body type are sparse; capillaries may be numerous or scanty; erythrocytic extravasation is sometimes abundant, and deposits of hemosiderin may or may not be present.

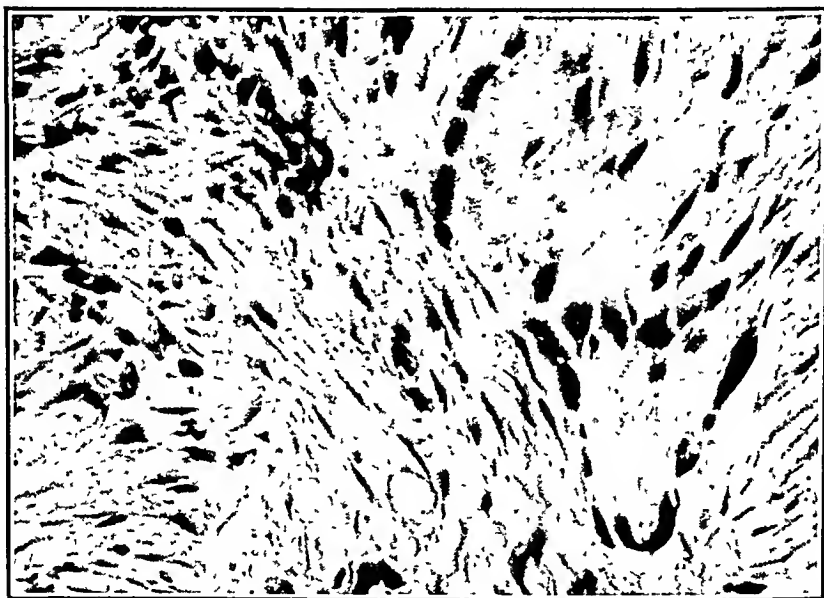


FIG. 102 —Ossifying fibroma of the maxillary sinus. There are intertwining bundles of fibroblasts and two spicules of bone surrounded by osteoblasts. x 200

This tumor should be *suspected* when a young patient, and particularly a girl, gives a history of a slowly progressing deformity of a cheek, hard palate or alveolar ridge. *Roentgenograms* will show a smooth non-infiltrating opacity the density of which will depend upon the amount of calcification. *Treatment* is surgical removal. *Recurrences* occur in less than 15 per cent of cases.

Carcinoma.—Carcinoma of the nose and paranasal sinuses is a most distressing disease not only because of its proximity to the eye and brain but also because of its inaccessibility. It affects males twice as frequently as it does females and is usually found after the age of forty years. In cancer of the *nose*, *symptoms* consist of a recent nasal obstruction, increased discharge, bloody purulent discharge, bleeding following the slightest trauma or manipulation and dull persistent pain that is worse at night or upon lying down.

A diagnosis of carcinoma should be suspected when a patient presents the signs and symptoms listed above. Bony erosions seen roentgenographically are quite suggestive. The diagnosis must always be confirmed histologically. *Treatment* consists of combinations of electrocoagulation, surgical excision and irradiation. The *prognosis* is somewhat better in the more anaplastic growths for these are more radiosensitive and it is frequently impossible to remove all the tumor surgically. The tumor *spreads* by local extension and by metastasis to the regional lymph nodes and rarely to distant organs.

Mechanical Disturbances—Mechanical disturbances of the nose and sinuses are the concern of the rhinologist and are of little interest to the surgical pathologist. They will, therefore, not be considered in detail.

Trauma—Trauma to the nose and sinuses is usually direct and frequently results in compound fractures. In the nose the site of the injury is more often confined to the cartilage or to the junction of the cartilage with bone. There are immediate hemorrhage, marked swelling and a deformity that depends upon the extent of injury. Fractures of sinuses are perhaps less common. The maxillary sinus is involved more frequently than the frontal or ethmoidal cells. In the former there may be a deformity of the cheek and upper jaw and injury to the teeth, whereas the latter may be accompanied by rhinorrhea or meningitis. In each the most common complication, however, is sinusitis. *Treatment* depends entirely upon the extent of the injury. If the deformity is minimal it should be left alone, otherwise an attempt should be made to replace the fractured segments.

Hemorrhage—Hemorrhage from the nose is known as *epistaxis*. It is a symptom and not a disease. In 90 per cent of cases its point of origin is the vascular area in the anterior portion of the cartilaginous septum. Its *causes* are protean. Briefly they may be divided into general conditions such as hypertension or blood dyscrasias and local disturbances. The latter may be grouped into (1) hereditary as hereditary hemorrhagic telangiectasia, (2) infections as syphilis, tuberculosis or any inflammatory process attended by ulceration, (3) neoplasms particularly ulcerating carcinoma and less often polyps and (4) mechanical disturbances such as trauma or foreign bodies. It should also be pointed out, however, that nose bleeds, without apparent cause, are not infrequent in children up to the age of puberty at which time they tend to disappear spontaneously.

Foreign Bodies—Foreign bodies of the nose usually enter by the nares or through the lateral wall although sometimes they are formed within the nasal cavity. *Extraneous* foreign bodies are found more frequently in children than in adults, and consist of virtually any material that the child can insert into the nose. Some of the more common objects are buttons, coins, pins, vegetables, sticks, pencils and screws. Similar objects may be found in the nose of a mentally deficient adult, although ordinarily foreign bodies in the nasal cavity of an adult comprise missiles from firearms and

they impart a xanthoma-like appearance to the stroma. *Anaplastic carcinomas* vary considerably morphologically. In general they are of two varieties—round or spindle and they therefore resemble sarcomas (Figs. 104 and 105). In fact many cases described in the literature as examples of the latter are doubtlessly anaplastic carcinoma. As in squamous cell carcinoma if sections are obtained at the correct level, neoplastic cells are seen to arise in the deep portion of the covering epithelium. They infiltrate the underlying tissue singly in a manner similar to inflammatory cells, in small cords, or in diffuse sheets. The cells are comparatively small,

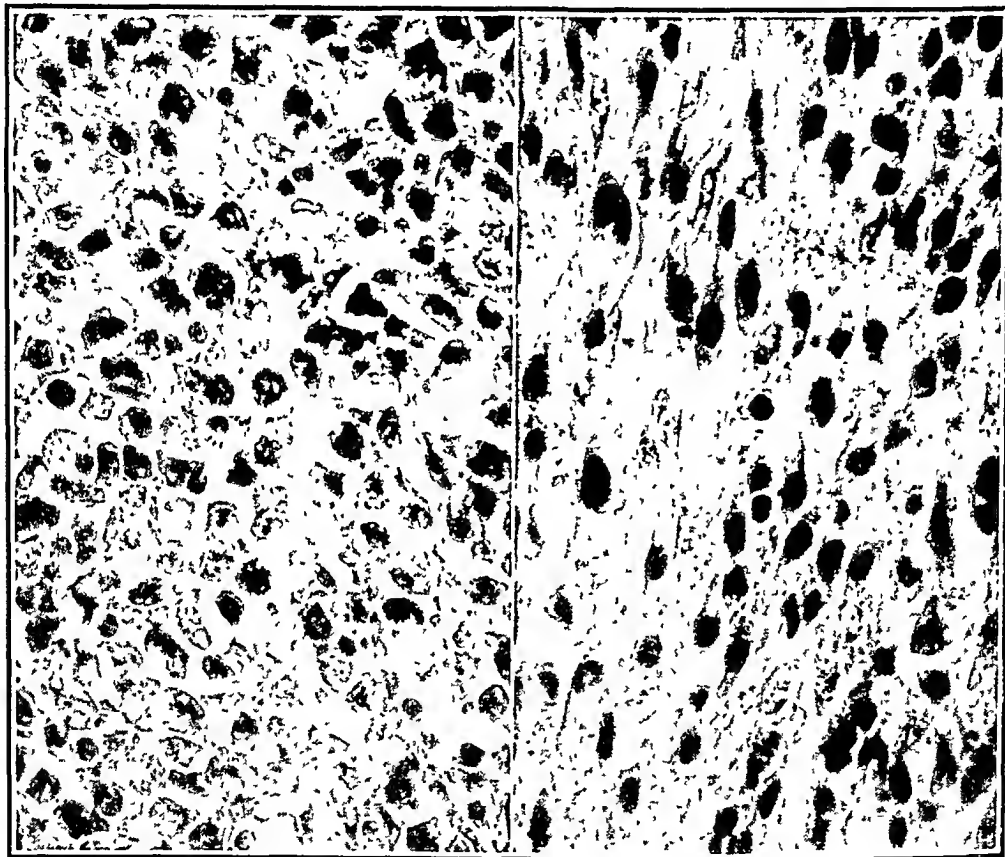


FIG 104

FIG. 105.

FIG. 104 —Anaplastic carcinoma of the nose. There are numerous irregular single cells with scanty cytoplasm and bizarre nuclei. x 400.

FIG 105 —Anaplastic carcinoma of the nose showing numerous elongated cells. In other areas of the same tumor carcinomatous characteristics were well developed. x 400

round, polygonal, elongated and spindle shaped, or irregular. They have a scanty or moderate amount of solid or sometimes granular eosinophilic and less often basophilic cytoplasm. The nuclei are also variform. They are small, round, triangular or irregular and are either vesicular or intensely hyperchromatic. Nucleoli are sometimes conspicuous. The stroma may be abundant, dense and fibrous and when it contains solid cords of cells between its stout meshes it imparts a cylindromatous appearance to the tumor. Frequently, however, it is less abundant, more cellular, and is rich in engorged capillaries.

this is sucked in as the air re-enters the sinus and results in infection. Even more frequently, however, a redundant ostial mucosa may act as a baffle allowing air to escape from, but not re-enter, a sinus. This produces a vacuum, pulls the epithelium away from the bone, and results in a hematoma of the tumor propria. The incidence of aer sinusitis is about 3 per cent of those in flights over 25,000 feet. The larger sinuses, namely, the frontal and maxillary are sites of predilection and the seasons closely parallel those of acute infections of the nose and pharynx. Pain over a sinus developing during or shortly after a flight readily establishes the diagnosis. Treatment is symptomatic. Rarely is operation necessary. Prophylactically, personnel with obstructed ostia or with acute nasopharyngitis should not be permitted to make high altitude flights.

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surgical apparatus such as gauze, sponges and instruments left behind as a result of treatment. *Symptoms* consist of pain, sneezing, unilateral fetid discharge, bleeding and obstruction. Pathologically they produce varied degrees of chronic inflammation and ulceration. *Treatment* consists of removing the object. Foreign bodies *formed within the nose* are known as *rhinoliths* or stones. They are usually composed of calcium phosphate and carbonate, form around a nucleus of blood and mucus or around a foreign body, weigh as much as 11 gm., are unilateral, occur more frequently in adults, and affect women four times as often as they do men. *Symptoms* consist of unilateral lacrimation, nasal obstruction and discharge. Clinically, they must be differentiated from bony sequestra, calcified polyps and osteoma. *Treatment* is removal either by way of the nostril or by lateral rhinostomy.

Foreign bodies of the *paranasal air sacs* affect the maxillary sinus most frequently and the ethmoid, frontal and sphenoid sinuses only rarely. They are almost always deposited as a result of trauma or surgical procedures, although exceptionally they may enter through the ostia. The most frequently encountered *objects* are roots of teeth, parts of instruments, bullets and shrapnel. Their importance lies in the fact that they carry with them bacteria which result in a sinusitis. Sometimes the infection is minimal and the object is walled off, but at other times it is more severe and results in supuration. The *diagnosis* is obtained by taking a careful history, by performing a thorough examination including that of the mouth, and by roentgenography. *Treatment* is removal through the route it entered, through a naso-antral opening or through a Caldwell-Luc incision.

Cerebrospinal Rhinorrhea.—Cerebrospinal rhinorrhea is escape of spinal fluid through the nose. The *causes* may be listed as follows: (1) *Congenital* such as nasal encephalomeningoceles and internal hydrocephalus. (2) *Inflammatory* including non-specific chronic sinusitis or granulomatous infection of the sinuses such as syphilis, tuberculosis and leprosy. (3) *Tumors*—particularly those of the pituitary gland and osteoma of the frontal and ethmoid bones. (4) *Trauma*: This includes accidental fracture of the skull or following operations upon the paranasal sinus or cranium. (5) *Idiopathic*: *Symptoms* consist of continuous or intermittent escape of clear watery fluid from one or both nostrils. The amount varies to as much as two liters in twenty-four hours. The fluid does not excoriate the skin, does not produce stiffening of a handkerchief when allowed to dry and, upon examination, discloses all the findings of spinal fluid. *Treatment* depends upon the cause. Some patients recover spontaneously while others are treated surgically. The danger of an ascending infection is always present and the *prognosis* must, therefore, be guarded.

Aerosinusitis.—Aerosinusitis is a comparatively new disease that has eventuated as a result of high altitude flying and less often as a result of deep sea diving. If the ostia are normally patent the air pressure within a sinus is readily equalized in ascent and descent. If, however, the aperture is covered with an infected film of mucus

Chapter IV

LARYNX

EMBRYOLOGY

THE *larynx*, along with the trachea and bronchi which are described in the ensuing chapter, arises from the entodermal tube resulting from the formation of a median longitudinal laryngo-tracheal groove. The *epiglottis* is apparent in the 5 mm embryo as a mid-ventral swelling of the third and fourth arches. It soon develops a transverse flap and about the fourth month of embryonic life it acquires its cartilaginous support. The *primitive glottis* is represented by a longitudinal slit in the floor of the pharynx that represents the persistent anterior part of the original laryngo-tracheal groove. It is bounded laterally by condensations of the fourth and fifth arches called arytenoid swellings. As these grow cephalically they meet the epiglottis and at the seventh week they convert the slit into a T shaped cleft. The surfaces of the cleft, however, become adherent and close off the aperture until the tenth week when they dissolve to re-open the lumen. At the same time a pair of lateral recesses, the laryngeal *ventricles*, become apparent. They are bounded above by a pair of bands known as ventricular folds or false vocal cords, and below by another pair called true vocal cords. The laryngeal cartilages and muscles make their appearance in the seventh week of embryonic life as condensations of mesenchyme of the fourth and fifth arches.

ANATOMY

The *larynx* is situated at the upper and anterior part of the neck opposite the third, fourth, fifth and sixth cervical vertebrae. It is the same size in both sexes until the time of puberty when the male organ develops at a greater rate than does that of the female. In men the length is 44 mm, the transverse diameter is 43 mm and the anteroposterior diameter is 36 mm. In women the respective dimensions are 36 mm, 41 mm and 26 mm. The shape of the larynx is imparted by nine cartilages—1 thyroid, a cricoid, and epiglottic, two arytenoid, two corniculate and two cuneiform, which are bound together by ligaments, membranes and muscles. The laryngeal aperture is represented anteriorly by the upper edge of the epiglottis, on each side by the aryepiglottic folds, and posteriorly by a fold stretched between the arytenoid cartilages. The vestibule is that part of the larynx between the aperture and the ventricular folds. Recesses immediately inferior to the latter are called the *ventricles*, and extending superiorly from each of these is a sac known as the *ventricular appendix*. Below the ventricles there are two anteroposterior folds—the *true vocal cords*. The lower part of the laryngeal cavity extends from the level of the vocal cords to the upper part of the trachea with which it is continuous. The laryngeal branches

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cords The *lesion* eventuates from a failure of dissolution of the adherent surfaces of the primitive cleft which normally separate during the tenth week of embryonic life. In three fourths of the cases the web is found at the level of the vocal cords, in most of the others it is located subglottically, and only in a few is it situated supraglottically. The size varies from a rounded anterior commissure to complete atresia. The membranes are greyish white, glistening and wedge shaped. During inspiration, the upper surface is flat, smooth and stretched and the posterior border is thin, sharp and concave, but during phonation the web may fold above or below the cords. *Histologically*, it consists of a core of vascularized connective tissue covered on the upper surface with stratified squamous epithelium and on the under surface with ciliated pseudostratified columnar epithelium. The lesion is found in both sexes with equal frequency, is usually discovered before the age of thirty years and is associated with other congenital anomalies in 12 per cent of cases. *Symptoms* depend upon the degree of obstruction and may consist of hoarseness, dyspnea, and a weak or high pitched voice. In addition to these, infants may disclose stridor, cyanosis and difficulty in feeding. In adults it may be difficult to differentiate a congenital web from one acquired as a result of trauma or infection. The *diagnosis* is made by direct laryngoscopy. *Treatment* is indicated only when there is serious interference with respiration and consists of incision or excision. The *results* are often disappointing.

Laryngeal Cysts—Some cysts of the larynx are congenital whereas others are acquired. Both are included here for the sake of convenience. *Acquired* cysts may be true—resulting from occlusion of the ducts of the glands brought about by inflammation or trauma or they may be false—due to extravasation of blood into the connective tissue of the tunica propria with subsequent encapsulation. They are located in the epiglottis, vocal cords, lateral wall of the larynx or the aryepiglottic folds and are not usually found in infancy or childhood. *Congenital* cysts probably arise from displaced embryonal cells which normally form the appendix of the ventricle. Consequently, they are found in the lateral wall of the larynx or near the aryepiglottic folds. They occur at all ages. Their size varies from a few millimeters to 3 or 4 cm. in diameter and as a rule they become much larger than do the acquired cysts. Otherwise congenital and acquired occlusion cysts are similar *grossly* and *microscopically*. The walls are usually thin and they contain serous gelatinous or colloid material. *Histologically*, the lining in each is initially ciliated pseudostratified columnar but later it may become attenuated, undergo metaplasia to a stratified squamous type or it may even disappear (Fig. 106). The tunica propria contains elastic tissue, lymph follicles and lymphocytes. Except when *complicated* by hemorrhage or infection the growth of laryngeal cysts is gradual so that they may occlude most of the airway and yet produce few or no *symptoms*. When present the latter may consist of dyspnea, hoarseness, cough, fullness in the throat and difficulty in swallowing. *Diagnosis* is made by direct laryngoscopy which reveals a smooth shining, semitransparent, tense, cystic mass that is com-

of the superior and inferior thyroid arteries constitute the chief *arterial* supply. The *lymphatic* vessels follow the arteries and drain into the deep cervical nodes which are located along the carotid sheath from the base of the skull to the root of the neck. The *nerves* are derived from the internal and external branches of the superior laryngeal nerve, from the recurrent laryngeal nerves and from the cervical sympathetics.

Histologically, the lining of the upper part of the larynx to the level of and including the vocal cords is of a stratified squamous variety. Below the vocal cords it is of a ciliated pseudostratified columnar type. A tunica propria of loose connective tissue contains mucous and serous glands, blood and lymph vessels, nerves and in some areas, as in the region of the vocal cords, bands of elastic fibers. The deeper structures consist of striated muscles, cartilages covered with perichondrium and ligaments.

PATHOLOGY

Congenital Anomalies—Developmental abnormalities of the larynx consist of hypoplasia, asymmetry, aplasia, stridor, web, cyst and laryngocele. Only the latter four are frequent enough and of sufficient clinical interest to merit separate consideration.

Congenital Stridor.—Congenital laryngeal stridor is the most common stridor in infants. It has *also* been *called* infantile respiratory spasm, congenital laryngeal obstruction, respiratory choking in babies, infantile laryngeal spasm and clonic spasm of the glottis. An otherwise normal infant develops *noisy breathing* shortly after birth. It consists of a croaking sound during inspiration which gradually increases in pitch. Expiration may or may not be associated with a short low pitched crow. The sound is usually audible during waking hours and sometimes even during sleep. It is intensified at the time of emotional or physical excitement. It is not accompanied by cyanosis or respiratory distress, although there usually is indrawing of the thoracic cage. The intensity of the noise increases for a few months after birth, remains stationary for a few months and disappears spontaneously during the second year. The condition is *due to* an exaggeration of a normal infantile type of larynx which is characterized by flaccidity of the structures that compose the laryngeal aperture. The stridor results from vibrations of a flabby epiglottis folded back across the larynx and of unsupported aryepiglottic folds both of which are sucked in during inspiration. The disorder should be *differentiated* from a small glottic lumen, a congenital web, congenital cysts, micrognathia, macroglossia and foreign body. The *diagnosis* is made by direct laryngoscopy. *Treatment* is unnecessary and the *prognosis* is good.

Congenital Web.—This anomaly is not rare for the literature contains over 130 cases and there are doubtlessly many others that have not been reported. Some of the *synonyms* are: congenital glottic stenosis, pseudomembranous stenosis, diaphragm, congenital laryngeal stenosis, cicatricial stenosis, congenital membrane, congenital occlusion, laryngeal stenosis and membranous synechia of vocal

ing at stools. If the swelling is internal it may produce hoarseness and if it is external its only *symptom* may be discomfort in the neck. *Treatment* is excision. The *prognosis* is good.

Inflammation — Non-Specific Inflammation — Acute Laryngitis — Acute inflammation of the larynx is a common complication of acute rhinitis and pharyngitis and is not the concern of the surgeon unless it produces obstruction to the airway. Since the occlusion of the laryngeal lumen is usually due to concomitant edema and since edema may occur in the absence of a pre-existing infection it would perhaps be more fitting to speak of the condition as edema of the larynx with and without inflammation. The *causes* of edema are protean and may be divided into (1) those accompanying infections such as acute rhinitis, pharyngitis or tonsillitis, Ludwig's angina, influenza, typhoid fever, diphtheria, scarlet fever, measles, small pox, erysipelas, tuberculosis, glanders and syphilis, (2) neoplasms interfering with venous return to the heart, (3) mechanical disturbances such as foreign bodies, fracture of the larynx and inhalation of steam and irritating gases, and (4) general conditions including allergic disorders, cardiac failure, renal diseases and pulmonary diseases. There is, of course, no predilection for either sex but the age groups vary according to the causative factor. Thus *infants* are the usual victims in edema arising as a result of acute infections of the upper respiratory tract, exanthemata and foreign bodies, whereas adults are more frequently affected in edema resulting from inhalation of irritating substances, from neoplasms and from the general conditions listed above. *Symptoms* may be abrupt without preliminary warning or they may occur gradually. There may be hoarseness, cough, dryness, tickling, wheezing, stridor, asphyxia and when obstruction becomes more complete cyanosis and indrawing of the suprasternal notch, abdomen and ribs.

Examination of the larynx by mirror or direct laryngoscopy reveals a pink to fiery red and dull mucosa in the presence of an accompanying inflammation or a paler more glistening surface in the absence of infection. There is in addition swelling of the epiglottis, the aryepiglottic folds, the ventricular bands and the vocal cords producing rounded, edematous, soft boggy structures that protrude into the laryngeal lumen and encroach upon or entirely obliterate the airway. *Histologically*, in cases of non-inflammatory origin, there is maximum collection of edema fluid in the submucosa with little or no infiltration with inflammatory cells. In cases of inflammatory origin the epithelium may be intact or partially or wholly denuded. The surface may be clean or covered with an admixture of sloughed epithelial cells, fibrin and leukocytes. In addition to edema fluid the submucosa discloses an engorgement of capillaries, varying numbers of neutrophils, plasma cells, lymphocytes and eosinophils and marked activity of the submucosal glands.

The *diagnosis* is suspected upon eliciting the signs and symptoms enumerated above and it is easily confirmed by mirror or direct laryngoscopy. *Treatment* consists of keeping the airway open (by tracheotomy if necessary), of removing the cause and in cases accompanied by inflammation of chemotherapy. The *prognosis* depends

pressible with a probe. *Treatment* of small cysts is removal laryngoscopically whereas that of larger cysts is extirpation by way of thyrotomy. The *prognosis* is good.



FIG. 106.

FIG. 107.

FIG 106 —Cyst of the larynx filled with eosinophilic precipitate and lined with a double layer of cuboidal cells x 100.

FIG. 107.—Chronic hypertrophic laryngitis showing slight keratinization of the surface epithelium and increased fibrosis, edema, vascularity and plasma cell infiltration of the tunica propria x 200.

Laryngocele.—A laryngocele is a hernia or an air sac that sometimes develops from the appendix of the ventricle. It is rare in man but is common in frogs, birds and some apes where it serves as a reserve supply of air. The lesion itself is acquired but a predisposition for its *development* is congenital and exists in the form of a long appendix. During strenuous exercise of the upper extremities, when straining at stools or in initiation of coughing the glottis is closed. This is accomplished by closure of the true vocal cords and the muscles of the upper aperture of the larynx. The intratracheal pressure is increased but because closure of the true vocal cords is less effective than that of the muscles the force is transmitted to the ventricles. When the appendix is short its wall gains support from the thyro-arytenoid muscles but when it is long and stretches beyond these muscles the support is lost resulting in a predisposition to herniation. The *lesion* is found more frequently in young children and in women than it is in men. Its most common location is within the larynx above the ventricular folds and extending to the ary-epiglottic folds or the base of the tongue. Sometimes the herniation perforates the hyoid bone and appears as a swelling in the neck. In either case the sac enlarges on forced expiration, coughing or strain-

ing at stools. If the swelling is internal it may produce hoarseness and if it is external its only *symptom* may be discomfort in the neck. *Treatment* is excision. The *prognosis* is good.

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The *diagnosis* is suspected upon eliciting the signs and symptoms enumerated above and it is easily confirmed by mirror or direct laryngoscopy. *Treatment* consists of keeping the airway open (by tracheotomy if necessary), of removing the cause and in cases accompanied by inflammation of chemotherapy. The *prognosis* depends

upon the age of the patient, the causative factor and the severity of involvement.

Chronic Hypertrophic Laryngitis.—This condition results from *trauma* to the vocal cords, as for example from shouting, or from repeated attacks of laryngitis. The only *symptom* is dysphonia. *Laryngoscopy* discloses a round thickening of one or both vocal cords throughout their membranous portion. The normal pink color is replaced by a fusiform, irregular, reddish sometimes edematous band. The inflammation may involve the ventricular bands and occasionally the entire larynx. The surface may be covered with tenacious secretions. *Histologically*, the epithelium discloses some keratinization and hypertrophy. The principal changes are in the tunica propria in the form of edema, increased vascularity, a diffuse infiltration with plasma cells and lymphocytes, and a striking deposit of fibrous tissue that extends to the muscle layers (Fig. 107). *Treatment* consists of stripping the mucosa and excess tissue away from the cords and allowing the epithelium to recover the surface by regeneration. The *results* are good.

Specific Inflammation.—Most chronic granulomatous lesions of the larynx are too uncommon to deserve more than a passing comment. In general, if the lesions are located on the vocal cords they will produce hoarseness relatively early, but if they are situated in other portions of the organ *symptoms* occur late in the disease and consist principally of obstruction to the airway. *Scleroma* has been considered in the preceding chapter. It is usually a disease of the nose and nasopharynx and only secondarily does it involve the larynx. On rare occasions, however, it may originate in the larynx. The *lesion* is located subglottically as a pale red, grey, or white smooth mass that extends to and compresses the vocal cords. Sometimes, however, the supraglottic area may be attacked first. The microscopic changes are the same as those already described. *Glanders* almost always involves the larynx secondary to a lesion in the nose and nasopharynx. It produces an infiltration and then ulceration and necrosis of the laryngeal mucosa and cartilages. It may be accompanied by considerable edema. *Leprosy* of the larynx is never primary. The disease is found in the epiglottis, aryepiglottic folds, and ventricular bands as an extension from the upper respiratory tract. It exists as an infiltrating, nodular, ulcerating and cicatrizing lesion that produces severe distortion of the organ and reduces its lumen to a narrow opening. The histologic changes are similar to those described in the section on the skin. *Boeck's sarcoid* rarely affects the larynx. More frequently it is part of a general disease but occasionally it is primary. The lesion exists as a rounded, firm, nodular mass located beneath the mucosa. *Histologically*, it consists of the usual hard tubercles that are so characteristic of this disease. *Actinomyces* is rare in the larynx. It exists as a painless hard mass in the recess between the larynx and the pharynx and usually represents a direct extension from the jaw. It may be confused with carcinoma.

Tuberculosis.—Tuberculosis of the larynx is relatively common. It is almost always *secondary* to pulmonary tuberculosis and is

caused by mycobacterium tuberculosis of either the bovine or human strains. The usual *route* of invasion is implantation from sputum by way of the ducts of the submucosal glands or through an ulcerated or intact mucosa. Rarely, however, its presence in the absence of tuberculosis in the lungs and in the absence of tubercle bacilli in the sputum indicates a hematogenous method of origin. It is found in from 20 to 30 per cent of patients with clinically evident disease and in from 40 to 50 per cent of all tuberculous patients coming to necropsy. In cases with laryngeal involvement there is an unequivocal increase in specific infection of the tracheo-bronchial tree and of the intestines. It is found with equal frequency in both sexes and all races and is most common between the ages of twenty and forty years. Since early *symptoms* are scarce the larynx of patients with tuberculosis should be examined at frequent intervals. There



FIG. 108.—Widespread tuberculosis of the larynx

may be dryness, burning or irritation in the throat, hoarseness, cough, pain and later dyspnea.

The precise *location* and appearance of the lesions can be well visualized by minor or direct laryngoscopy, and, of course, at necropsy. Statistics vary with regards to the most frequent sites of involvement although the three most commonly affected structures are probably the vocal cords, the epiglottis and the ventricular bands. Any portion, however, and sometimes the entire surface may be involved (Fig 108). The lesions may be single or multiple and less than a millimeter or several centimeters in diameter. Early they exist as hyperemia, edema and simply thickening of the mucosa but later they appear as nodules and as superficial or deep ulcerations. Initially the ulcer is shallow, irregular and measures as much as 5 mm in diameter. As it becomes older it maintains its irregular

shape but it becomes deeper, is lined with yellow or grey necrotic and friable tissue and it develops overhanging and undermined edges. It may destroy all the underlying tissue down to and including the cartilages, and may extend inferiorly to the trachea and superiorly to the base of the tongue. *Histologically*, the earliest changes occur in the submucosa and are non-specific but the ensuing specific alterations are characteristic tubercles composed of epithelioid cells, Langhans' giant cells and about the periphery lymphocytes and a few plasma cells (Fig. 109). There may or may not be central caseation necrosis. As the tubercles enlarge and coalesce they encroach upon, attenuate and ultimately break through the covering epithelium to produce mucosal ulcers. As seen grossly the edges of the epithelium are undermined and tend to fall in. The surface of the ulcer is covered with caseous material beneath which there is a zone of tuberculous granulation tissue composed of capil-

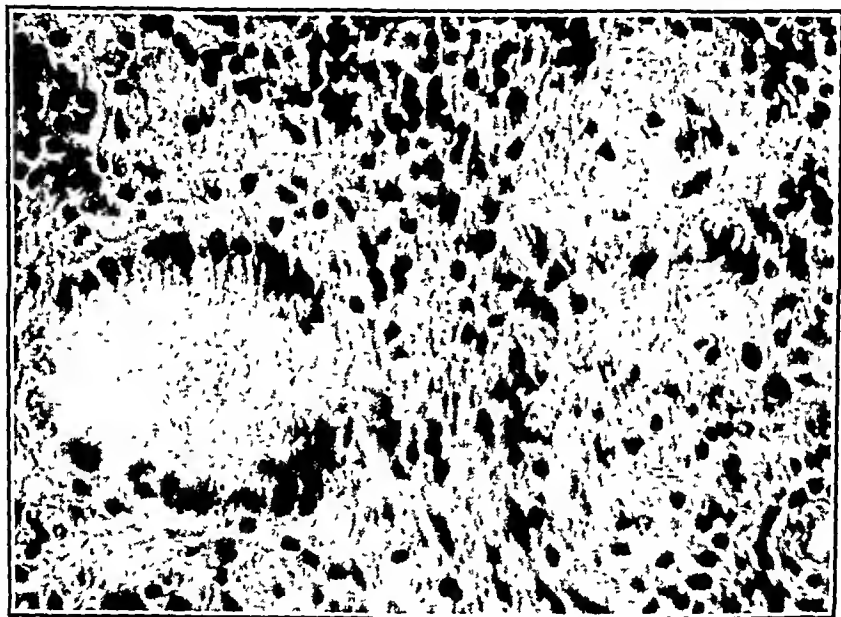


FIG. 109 —Tuberculosis of the larynx illustrating tubercles of epithelioid cells and a Langhans' giant cell. x 200.

laries, epithelioid cells, giant cells and some fibroblasts. Tubercles may or may not be apparent. The lesions *progress* by extension of the ulcer with destruction of all tissues that lie in its path. *Healing* is indicated by the walls becoming smooth, by granulations becoming more exuberant, by an increase of fibrosis and by a regeneration of the surface epithelium to cover the defect. Subsequent contraction of the fibrous tissue results in considerable distortion of the normal configuration of the larynx.

A *diagnosis* of laryngeal tuberculosis is made by direct or indirect laryngoscopic examination and by removal of tissue for histologic study when the lesion is not typical. Evidence of tuberculosis in the lungs or elsewhere in the body makes recognition easy and isolation of tubercle bacilli clinches the diagnosis. *Treatment*, consists of general and vocal rest, attention to the pulmonary and other lesions, proper diet and other anti-tuberculosis measures. Local electro-

cautery is advocated by some but condemned by others. The *prognosis* depends upon the extent of the primary lesion and the general condition of the patient. It is worse in children and males than it is in adults and females and it is somewhat better in the absence of ulceration.

Syphilis—Syphilis of the larynx is less frequent than it was formerly, probably because patients are being treated sooner. It is more common in men than in women and is usually of the *acquired* type. A *chancre* has been described on the epiglottis but is extremely rare. *Secondary* lesions in the form of diffuse inflammation or mucous patches are occasionally seen on the vocal cords and epiglottis during the eruptive stage. *Tertiary* lesions, however, are the most important. They may be located on the epiglottis, aryepiglottic folds, ventricular bands, vocal cords or any other part of the larynx and exist as a diffuse infiltration or as ulcerating gummas. The latter originate as submucosal nodules of varying sizes. They soften, break through the surface and leave deep, irregular, punched out, sharp craters covered with grey necrotic material and surrounded by inflammation and edema. They may extend to and destroy the underlying cartilages. Healing is accompanied by scarification, adhesions and distortion. *Histologically*, tertiary syphilis of the larynx is similar to that already described in the section on the skin. *Symptoms* depend upon the location and extent of the lesions. The most common is an alteration in the voice. Cough is rare, pain is not marked and dyspnea occurs late in the disease and only when the lesion is extensive. A *diagnosis* is made from the history, evidence of syphilis elsewhere, a positive blood Wassermann and a biopsy. The *prognosis* is good if treatment is instituted early.

Blastomycosis—Blastomycosis of the larynx is infrequently described in the literature, but the disease is probably more common than the few reports tend to indicate. It affects men more often than women and is usually found after the age of forty years. *Symptoms* consist of hoarseness of many months or several years duration followed by increasing dyspnea. *Laryngoscopic* examination discloses edema of the aryepiglottic folds, ventricular bands and vocal cords. The latter in addition reveal a granular or nodular surface covered with a grey exudate. As the process becomes older it is replaced with increasingly severe fibrosis resulting in distortion and complete stenosis of the laryngeal lumen. *Histologically*, the surface epithelium becomes greatly hyperplastic and sometimes ulcerated. The submucosa is at first quite vascular and diffusely infiltrated with plasma cells, monocytes and lymphocytes. Scattered sparsely there are pseudotubercles exhibiting giant cells that contain yeast-like fungi. Later the more active inflammation becomes replaced with dense fibrous tissue. The disease is frequently confused with tuberculosis. It can be *differentiated* by the fact that tubercle bacilli are not isolated, by the absence of tuberculosis in the lungs or other organs, by recovering the fungus in cultures on Sabouraud's medium and by biopsy. *Treatment*, consisting of tracheotomy because of obstruction and of administration of potassium iodide, is not satisfactory. The lesions usually extend to

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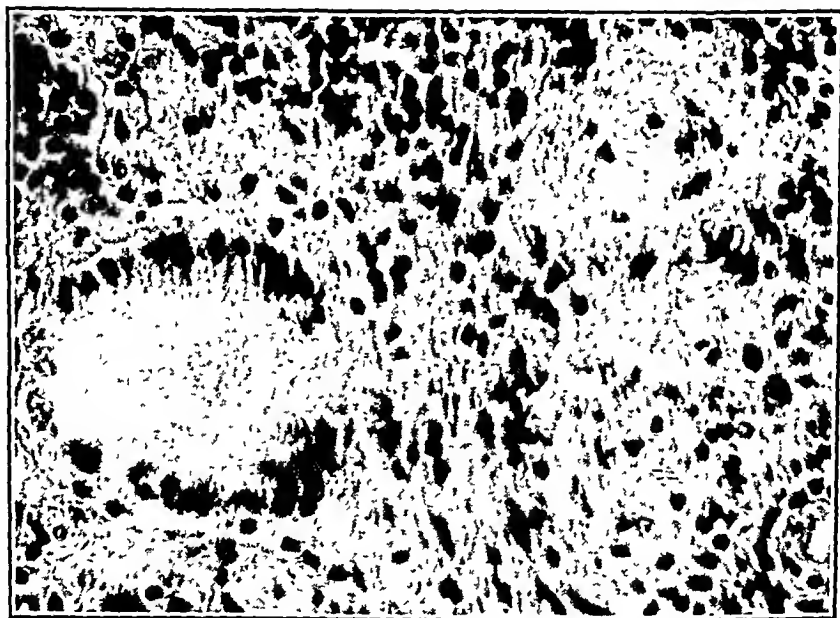


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Keratoses—Keratoses of the larynx is not a true neoplasm. It consists of localized, chalky white elevations on the upper surface and edge of the membranous portion of one or both vocal cords. It has also been called hyperkeratosis, leukoplakia and pachydermia laryngis. It affects adult males and, although the causes are unknown, its origin has been attributed to excessive smoking particularly of cigarettes, to abuse of the voice, to laryngitis and to deficiency in vitamin A. *Histologically*, the principal changes are found in the mucosa. They consist of a moderate or severe increase of keratin, of a hyperplasia of prickle cells and of a proliferation of basal cells to form projections into the underlying tunica propria (Fig 110). In most cases the basement membrane is distinct and

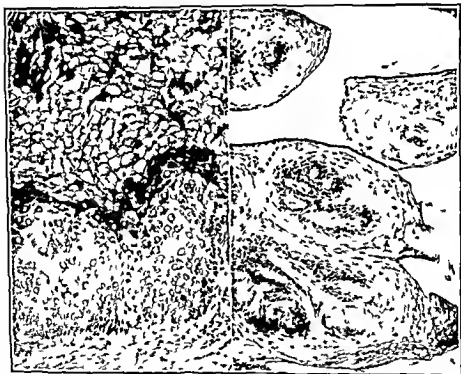


FIG 110

FIG 111

FIG 110—Keratoses of the larynx. There are an accumulation of keratin on the surface and a hyperplasia of the prickle cell layer. $\times 50$

FIG 111—Papilloma of the larynx showing hyperplastic stratified squamous epithelium covering thin stalks of loose connective tissue. $\times 50$

the arrangement of cells is quite orderly. In a few, however, the cells tend to become irregular so that it may be difficult to be certain whether the lesion is benign or malignant, whereas in occasional cases a transformation to a stratified squamous cell type of carcinoma is unequivocal. In all instances submucosal changes are inconspicuous and are of secondary importance. They are limited to the most superficial portion of the tunica propria and consist of some edema, a variable degree of fibrosis, thin capillaries, blood pigment and an infiltration with lymphocytes, plasma cells and monocytes. Keratoses is to be distinguished from chronic hypertrophic laryngitis

the trachea and the patients ultimately die from tracheal obstruction, pneumonitis and bronchiectasis.

Tumors.—Practically all tissues that are normally found in the larynx are capable of giving rise to a benign and a malignant tumor. From the surface epithelium there may develop keratosis, papilloma, basal cell carcinoma, Bowen's disease and squamous cell carcinoma; from submucosal glands cysts, adenoma, and adenocarcinoma; from connective tissue polyps, myxoma, fibroma, amyloid tumor and fibrosarcoma; from vessels a hemangioma, hemangioendothelioma, and lymphangioma; from nerves or nerve structures neurofibroma, neurofibrosarcoma, ganglioma and melanoblastoma; from muscle leiomyoma, leiomyosarcoma, myoblastoma and rhabdomyosarcoma; from perichondrium either directly or as a result of metaplasia chondroma, chondrosarcoma, osteoma, osteochondrosarcoma and myeloma; from fat lipoma; from connective tissue and fat fibrolipoma; from fat, connective tissue or reticulo-endothelial cells xanthoma, and from lymphoid tissue lymphoma and lymphosarcoma. In addition the larynx may be involved secondarily by tumors arising in the thyroid gland, esophagus, pharynx or other adjacent structures and rarely by metastatic tumors from distant organs. Many of the aforementioned neoplasms are so uncommon that the literature contains reports of but a few cases. These will be omitted from further discussion. Others, however, are frequent or important enough to be considered separately. These include such benign lesions as keratosis, papilloma, adenoma, polyps, amyloid tumor, hemangioma, neurofibroma and chondroma and only one malignant tumor—carcinoma.

In order to spare useless repetition it might be pointed out that *laryngeal tumors* whether benign or malignant present no characteristic or pathognomonic *signs* and *symptoms*. These will depend entirely upon the location of the tumor, and their duration will be in direct proportion to the rapidity of growth or enlargement. In general alterations in voice, hoarseness or aphonia will be caused by any lesion that affects the true vocal cords either directly or indirectly. They will appear relatively early when the tumor involves the cords primarily. Neoplasms involving other portions of the larynx are usually asymptomatic until they encroach upon the airway sufficiently to result in partial occlusion and dyspnea. This symptom, particularly in slowly growing tumors, is relatively late for the patient gradually accommodates himself to the ever decreasing lumen until the passage consists of a mere slit. Other symptoms of lesser importance are cough, fullness in the throat and pain. Since symptoms are not pathognomonic a correct *diagnosis* must depend upon a laryngoscopic examination supplemented by biopsy. *Treatment* of choice of all tumors whether benign or malignant is excision. When the growth is small this may be accomplished by removal with the aid of the laryngoscope, when it is larger by thyrotomy (laryngofissure) and when extensive by laryngectomy. The *prognosis* will depend, of course, upon the type of tumor, the degree of benignity or malignancy, the size and the presence or absence of metastases.

indicated not only by the long duration of the lesion without producing any metastases, but also by their characteristic microscopic appearance which is identical with some of the mixed tumors of the salivary glands and with some of the benign adenomas of the trachea and bronchi. They may be located in any portion of the larynx where there are mucous glands but actually the majority are found in the subglottic region. For this reason, and because they grow extremely slowly, symptoms consisting of dyspnea and hoarseness do not appear until late in the disease—not until the lumen is

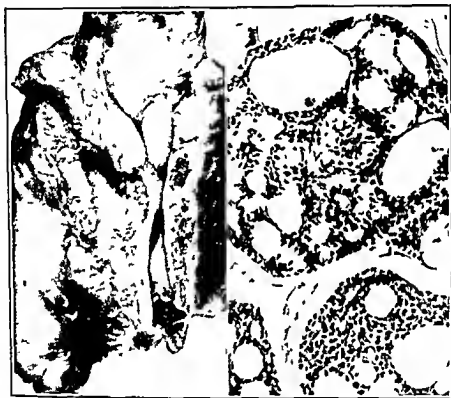


FIG 112

FIG 113

FIG 112—Adenoma of the larynx. The tumor is situated subglottically and is collar button like. The head occupies the luminal portion, the neck penetrates the wall and the base is located in the extralaryngeal tissues.

FIG 113—Section of the same tumor shown in fig. 112. The cells are uniform, have a moderate amount of cytoplasm and form a gland like arrangement. $\times 100$

almost completely occluded and the cords encroached upon from below. Grossly, the covering mucosa is glistening, smooth and not ulcerated. The submucosal part of the tumor is of varying dimensions but frequently reaches a diameter of 3 cm, an intermediate portion consists of a narrower neck that usually occupies the thickness of the laryngeal wall, and an extralaryngeal mass is often larger than the intralaryngeal portion (Fig 112). Ordinarily, the neoplasm is well demarcated and usually encapsulated but as it becomes larger it tends to infiltrate the adjacent tissues. It is extremely firm, solid and cuts like cartilage. Cut surfaces are

by the fact that the primary lesion in the former is found in the epithelium while in the latter it exists in the tunica propria. *Treatment* consists of vocal rest including cessation of smoking, of vitamin A therapy and of removal of the keratotic areas or of stripping the entire cord of the mucosa and submucosa. When malignant changes supervene the treatment is local excision or laryngectomy. If watched closely and treated correctly the *prognosis* is good.

Papilloma.—Papilloma is the most common benign tumor of the larynx. Two-thirds of the cases are found in children under twenty years of age and males are affected more frequently than females in the proportion of two to one. The disease is different in *children* than it is in adults. In the former it is self limited and disappears spontaneously after a few years or at puberty. The lesions are multiple—sometimes occupying the entire surface of the larynx and extending into the trachea and the mouth, they tend to recur promptly after excision and to implant on adjacent normal mucosa, and they never become cancerous. In *adults* the lesions may be single or multiple; they are frequently found on the vocal cords alone; they lack the tendency to recur after removal, and about 3 per cent become malignant.

The *tumors* are characteristically glistening, grey, pink or yellowish pink and mulberry-like. They have a finely granular or nodular surface, possess a sessile or pedunculated base, are not infiltrative or ulcerated, and measure as much as one centimeter in diameter. *Histologically*, they reveal a core of well vascularized loose connective tissue covered with hyperplastic and branched stratified squamous epithelium (Fig. 111). The surface of the latter contains a variable amount of keratin; the prickle cell layer is thick and composed of well differentiated polygonal cells, and the basal cell layer although regular and even frequently reveals hyperchromatism of the nuclei and often sends peg-like projections into the underlying connective tissue. The basement membrane is intact. Intranuclear inclusion bodies have been described in some epithelial cells; although in reviewing the histologic sections of cases on file in our own laboratory I have found no structures that could be thus construed. The *causative agent* in adults is unknown but in children it is thought by some to be a filtrable virus and by others to be an expression of a hormonal disturbance. Neither of these theories has been substantiated. *Treatment* is anything but standardized. In adults the lesions should be completely removed by excision or fulguration because of the danger of cancerous transformation. In children, although the need for removal is less pressing because of the tendency to spontaneous disappearance, they are nevertheless treated similarly. Tracheotomy is performed when the airway is obstructed. The *prognosis* should be guarded especially in young children in whom death may occur as a result of laryngeal obstruction.

Adenoma.—The literature is confused on the subject of adenoma of the larynx. A review of the available reports discloses that most authors consider a localized hyperplasia of submucosal glands as true adenoma, and that tumors which should be designated as such are often referred to as adenocarcinoma grade I. The latter is

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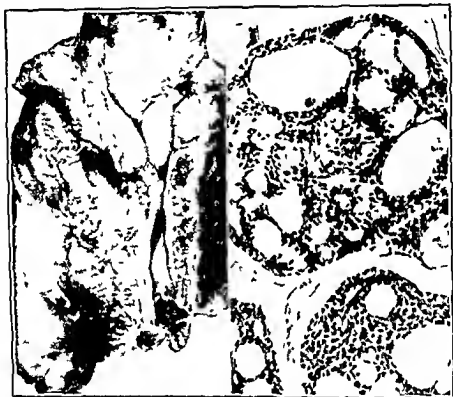


FIG 112

FIG 113

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in the larynx they usually involve the anterior two thirds of the vocal cords. Most frequently they are nodular, sometimes they are polypoid and occasionally they are pedunculated. They measure from less than a millimeter to 3 cm or more in diameter, are smooth, and appear grey, pink or red. *Histologically*, the surface epithelium is normal, attenuated, or hyperplastic. It may or may not show an increase of keratin. The submucosal portion is composed principally of connective tissue which may be dense and hyalinized, loose, or edematous to such a degree that fluid alone is apparent (Figs 114 and 115). Some polyps are vascular while others are replete with thin-walled capillary or cavernous spaces to a degree encountered in hemangiomas. Usually the vessels are engorged with erythrocytes but sometimes their lumens are plugged with recent or organized thrombi. Erythrocytic extravasation through-



FIG 116—Subglottic amyloid tumor. The tissue has been infiltrated with mass that takes a positive amyloid stain. $\times 200$

out the stroma is sometimes marked (probably as a result of trauma in removal) but leukocytic infiltration is never severe. Polyps are entirely benign. They never undergo a malignant change.

Amyloid Tumors—This is not a distinct tumor but is rather an infiltration of an existing tumor (usually a fibroma) with amyloid. Such neoplasms are always found in adults—usually between the ages of forty and fifty-five years. They exist as reddish colored, smooth, round, nodular, pedunculated or infiltrative firm masses that measure as much as 1.5 cm in diameter. They are located in the anterior two-thirds of the vocal cords, the ventricular bands, or the subglottic area. *Histologically*, they are composed of large masses of solid, wavy, hyaline-like material embedded in a dense collagenous fibrous tissue stroma (Fig 116). Amyloid is identifiable by the fact that it takes a positive iodine, methyl violet and congo red stain.

homogenously grey and hyaline in appearance. *Histologically*, these tumors are composed of sheets or masses of epithelial cells with round or oval foci of degeneration and liquefaction producing a gland-like appearance (Fig. 113). The cells are uniform, have an abundant or moderate amount of ill-defined basophilic or slightly acidophilic cytoplasm and round or oval regular evenly stained nuclei. The acinar spaces are empty, contain remnants of degenerating cells or are filled with stringy basophilic material. The supporting stroma is scanty or abundant, loose or fibrous and contains a variable number of blood vessels. The disease is treacherous

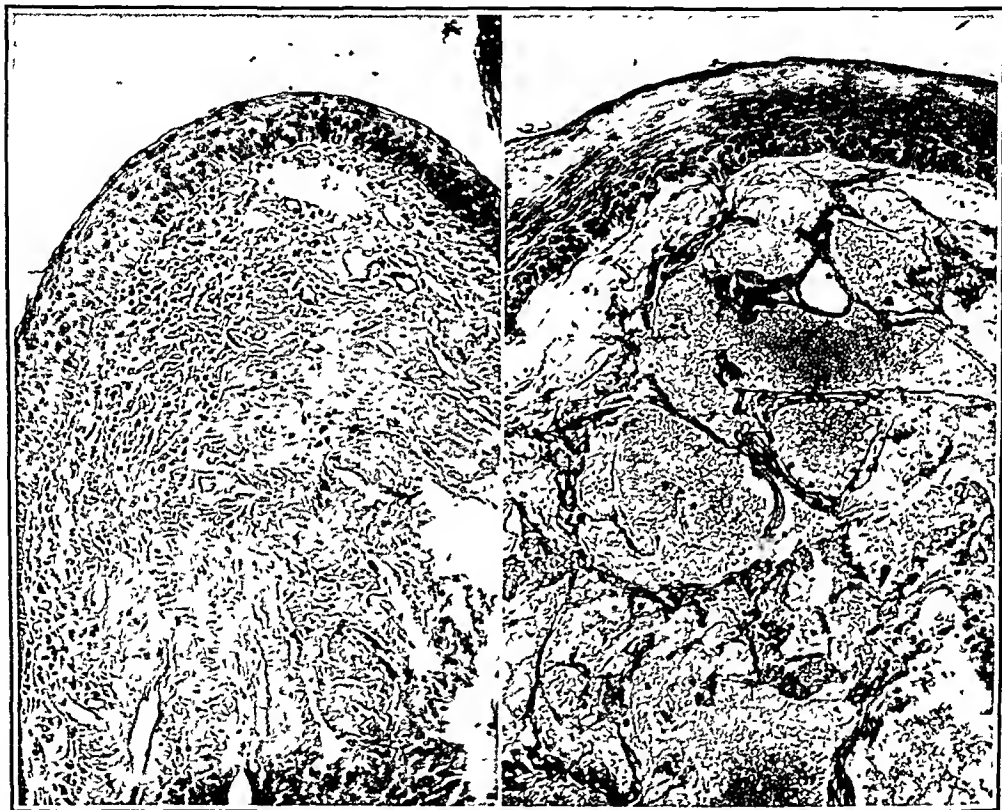


FIG. 114.

FIG 115.

FIG. 114.—Laryngeal polyp. The surface is covered with stratified squamous epithelium and the core is composed of hyalinized fibrous tissue x 50.

FIG. 115 —Laryngeal polyp. The epithelium is hyperplastic and the stalk contains numerous cavernous spaces filled with blood x 50.

because symptoms do not appear until late, because visualization of any tumor in the subglottic area is not always satisfactory, and because the firmness of the neoplasm makes biopsy difficult. Since the lesion remains localized for a dozen years, however, *complete excision* either locally or by laryngectomy should effect a cure in the majority of cases.

Polyps.—Polyps are not neoplasms in the true sense of the word and are included in this section only because they exist as tumor-like masses. They probably arise as a result of *inflammation* or *trauma*. They are always found in adults, affect men four times as frequently as women, and although they may be located anywhere

ages from six to fifty years and affects both sexes with equal frequency. It may be located in any portion of the larynx although its most frequent site is a ventricular band or an aryepiglottic fold. The size varies from a few millimeters to 3 or 4 cm. in diameter. The surface is smooth, the color is grey or yellowish red, and the consistency is firm. They are as a rule well encapsulated. *Histologically*, they are composed of interlacing bundles of spindle cells exhibiting a moderate or an abundant amount of cytoplasm and oval or spindle shaped, evenly stained nuclei. Palisading of the latter differentiates neurofibroma from simple fibroma (Fig 117). The treatment of choice is surgical excision and if all the tumor is removed it does not recur.

Chondroma—There are recorded in the literature approximately 85 cases of chondroma of the larynx. The tumor is found in males



FIG 118

FIG 119

FIG 118—Chondroma of the cricoid cartilage.
FIG 119—Histologic section of the same chondroma. $\times 200$

four times as frequently as it is in females, and although the most common ages are forty to sixty years, the youngest patient on record is fifteen years of age and the oldest is eighty-one. The lesion arises from the perichondrium of the inner surfaces of the laryngeal cartilages involving in decreasing order of frequency the posterior plate of the cricoid, the thyroid, epiglottis and arytenoid. Grossly, the tumor is fixed, solid protrudes into the lumen and extends externally, and measures from 1.5 to 6 cm. or more in diameter (Fig 118). The inner surface is convex, covered with a pink or congested mucosa and is occasionally ulcerated. Superiorly the subglottic tumor

Hemangioma.—Hemangioma of the larynx is not a rare tumor. Over 90 per cent of the cases occur in adults and two-thirds of all cases are found in males. The *cause* is unknown. Less than 10 per cent of the cases (those found in infants) are of congenital origin but the cause of those found in adults is not known. It is thought, without any proof, that severe cough, faulty use of voice and acute infection act as etiologic factors. In infants the disease is *manifest* by wheezing, labored breathing and obstruction. Symptoms are worse when there is a superimposed infection and periods of remission are characteristic. Examination may disclose cutaneous hemangiomata. In adults symptoms are vague, of long duration and typical of any laryngeal tumor. The most frequent *site* of the tumor in infants is the subglottic area whereas in adults it may be located on the vocal cords, ventricular bands, aryepiglottic folds

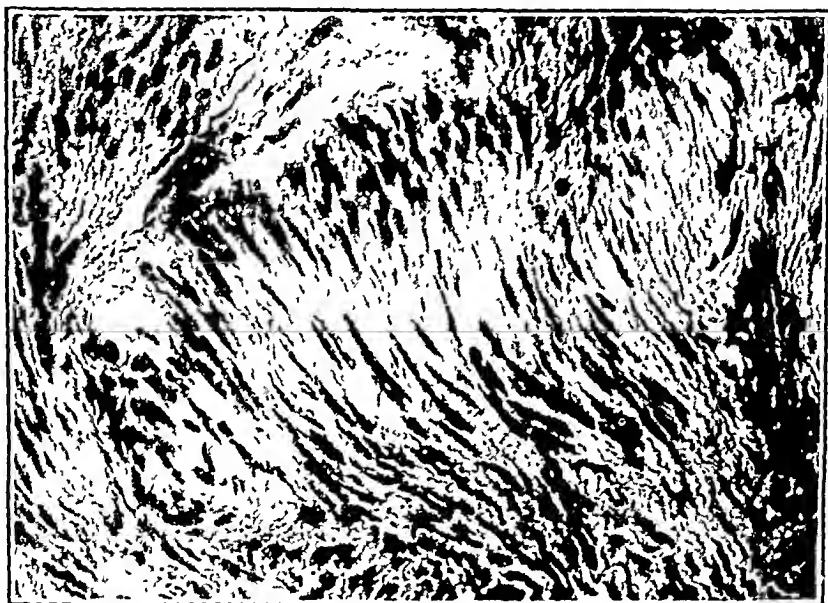


FIG 117.—Neurofibroma of the larynx showing conspicuous pallisading of the nuclei.
x 200

and epiglottis. The *neoplasm* may be a few millimeters or several centimeters in diameter. It may be present as a slightly raised fusiform elevation or as a polypoid mass possessing a sessile base or a narrow pedicle. The surface may be smooth, granular or nodular but it is rarely ulcerated. The color varies from purplish red to pink or white. *Histologically*, they are similar to cutaneous hemangiomas and are either of the capillary or cavernous type. The *diagnosis* is usually made by direct laryngoscopic examination. Biopsy, especially in infants, should not be resorted to because of the danger of uncontrollable hemorrhage. *Treatment* in infants consists of irradiation while in adults it is either irradiation or electrosurgical excision. Most of the infants whose cases have been reported in the literature have died from suffocation or hemorrhage. The *outcome* in adults, however, is considerably better.

Neurofibroma.—Neurofibroma of the larynx occurs as a solitary lesion or as part of a systemic neurofibromatosis. It is found at all



FIG 120

FIG 121



FIG 122

FIG 120—Early carcinoma of a vocal cord

FIG 121—Papillary carcinoma of the subglottic area

FIG 122—Advanced superficially ulcerating carcinoma of the epiglottis

(which is most common) encroaches upon the true vocal cords; inferiorly it extends into the trachea; posteriorly it compresses the esophagus, and anteriorly it occludes the airway. *Histologically*, it is composed of large round cartilage cells embedded in a hyaline or fibroelastic matrix (Fig. 119). The lesion may undergo calcification, ossification, myxomatous degeneration or sarcomatous transformation and it recurs if incompletely removed but it does not metastasize. The *prognosis* is good if all the tumor is extirpated.

Carcinoma.—Carcinoma of the larynx constitutes from 1.8 to 4 per cent of all malignant tumors of the body and it comprises 98 per cent of all malignant laryngeal neoplasms. It affects men fourteen times as frequently as it affects women and the most common age is between forty and sixty years. The *symptoms* are those of any laryngeal tumor and will depend, therefore, upon the location and size of the lesion. The *cause* of carcinoma of the larynx is not known but it is thought that the following play a contributory rôle; heredity, abuse of the larynx, smoking, inhalation of coal dust and gases, frequent attacks of laryngitis and hoarseness, pre-existing papilloma and keratosis, and testosterone. The latter is incriminated because of the marked preponderance of the diseases in males and because testosterone doubtlessly has some influence on normal growth of the larynx as witnessed by the change of voice at puberty.

Depending upon its location, cancer of the larynx is conventionally divided into *intrinsic* and *extrinsic* varieties. The former embraces all lesions that arise in or below the ventricles while the latter includes all growths that arise on or above the ventricular bands (Figs. 120, 121, and 122). An origin in a *vocal cord* accounts for two-thirds of all cases whereas the primary sites of the remaining third are equally divided among the subglottic region, ventricular bands, ventricles, aryepiglottic folds, arytenoids and epiglottis. In extracordal growths it is frequently impossible to establish the precise point of origin for by the time the patient is first examined the tumor already involves several anatomic structures. The *neoplasm* may be a few millimeters or 6 cm. or more in diameter. It may be papillary, or infiltrating and ulcerating. Papillary growths are sometimes difficult to distinguish from benign papillomas. They may be localized or disseminated. They are raised above the surface, roughly or finely granular, greyish white, superficially ulcerated and quite friable. Infiltrating growths produce a hard, ill-defined, thickening of the mucosa and submucosa. The tumor merges gradually with the adjacent normal tissue so that it is difficult to establish a line of demarcation between the two. As the lesion increases in size the central portion becomes elevated and ulcerated. The ulcer is sharply defined, irregular, has thick raised firm pink to grey often undermined edges, a floor covered with fetid necrotic grey material and a base of friable firm grey to white neoplastic tissue. The ulceration frequently extends to but does not completely destroy the underlying cartilages. *Histologically*, cancer of the larynx is, in the majority of cases, a stratified squamous cell type of growth. It may be entirely intraepithelial, but it usually exists as nests and

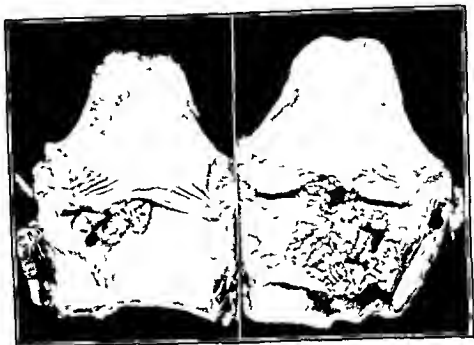


FIG 120

FIG 121:



FIG 122

FIG 120 —Early carcinoma of a vocal cord

FIG 121 —Papillary carcinoma of the subglottic area

122 —Advanced superficially ulcerating carcinoma of the epiglottis

cords of irregular cells that infiltrated the tunica propria (Figs. 123 and 124). The cells vary in shape and size although they are usually polyhedral. They have sharp cell boundaries, an abundant amount of eosinophilic cytoplasm and round oval or bizarre hyperchromatic nuclei. Mitoses are sometimes numerous and pearl formation may be prominent or inconspicuous. More undifferentiated growths are less common while completely anaplastic tumors are rare and are found almost entirely as extrinsic neoplasms. They exist as large sheets or diffusely infiltrating single round, oval or bizarre cells.

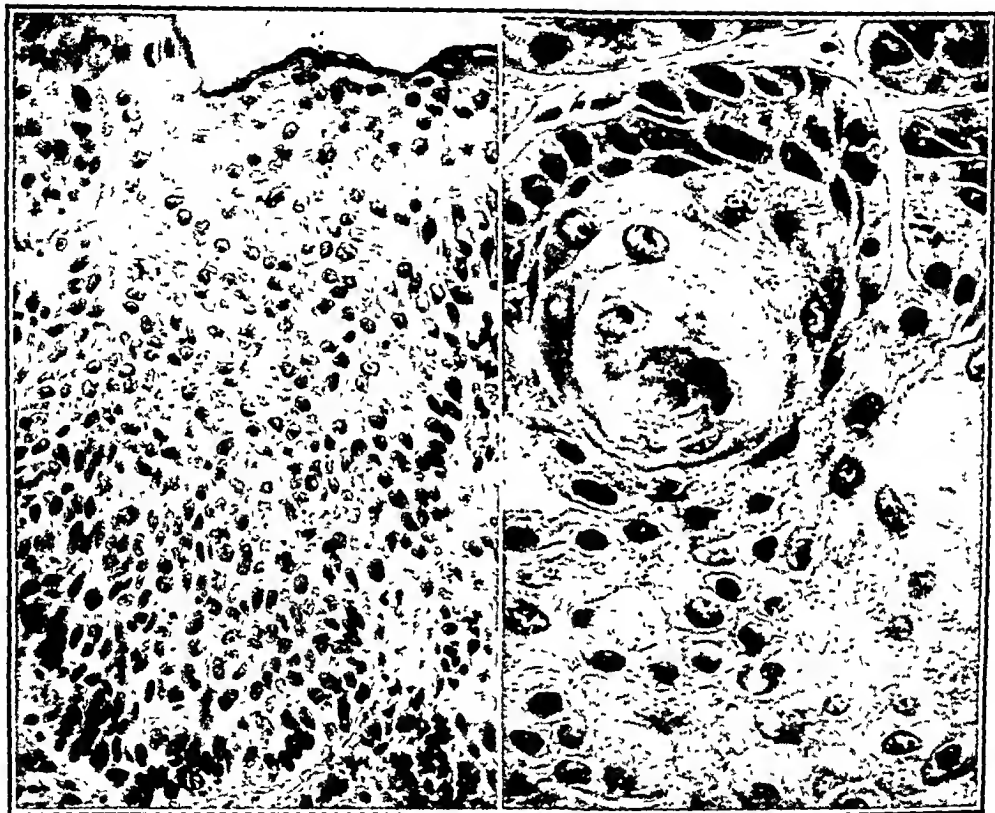


FIG. 123.

FIG. 124

FIG. 123 —Intra-epithelial carcinoma of a vocal cord. The basement membrane is still intact x 100.

FIG. 124.—Squamous cell carcinoma of the larynx showing a well formed epithelial pearl. x 200

Their margins are not always sharp; the cytoplasm is moderate or scanty and often somewhat basophilic, and the nuclei are bizarre, hyperchromatic and show varied mitoses. The supporting tissue in cancer of the larynx may be scanty or abundant, dense or edematous and is almost always infiltrated with plasma cells, lymphocytes and fewer neutrophils.

Cancer of the larynx *spreads* by contiguity, by the lymphatics and by the blood stream. By contiguity it extends in the sub-mucosal connective tissue and also intra-epithelially in a manner similar to Paget's disease of the nipple. This is especially true of the spread of carcinoma from one vocal cord to the other by way of the anterior commissure. Lymphatic spread to the carotid, sternomastoid and supraclavicular lymph nodes is more common in ex-

trinsic lesions than it is in intrinsic growths. Indeed in extrinsic neoplasms enlargement of the cervical nodes may be the first indication that something is amiss. It is because of this rapid spread that extrinsic tumors offer a poorer prognosis than do intrinsic ones. But lymphatic extension is not the only reason for early dissemination. Clerf has shown that solid cartilaginous plates offer a protective barrier to the spread of cancer from the vocal cords or the subglottic area, while the epiglottis and its lateral elastic membranes offer less resistance and allow extrinsic neoplasms to infiltrate the pre-epiglottic space relatively early (Fig 125). Metastasis of laryn-



FIG. 125.—Ulcerating carcinoma of the epiglottis extending into the pre-epiglottic space.

geal cancer by the blood stream is not common, but when it does occur any organ may be involved.

A diagnosis of carcinoma of the larynx is made from the history, by direct and indirect laryngoscopy and by biopsy. Treatment in most clinics is surgical excision either by local removal by way of thyrotomy or, if the lesion is more extensive, by laryngectomy and block dissection of the involved lymph nodes. Irradiation is usually employed in inoperable cases. More recently, however, good curative results are being reported by irradiation alone. In untreated cases the life expectancy is two years. Cures in patients whose lesions are early enough to be treated by local excision range from 50 to 80 per cent whereas cures in those needing laryngectomy are less than 50 per cent.

Mechanical Disturbances.—Foreign Bodies.—Aspirated foreign bodies are either coughed up or descend into the trachea and bronchi and are not commonly arrested in the larynx. The relative incidence of lodgement in these three sites is larynx 1, trachea 2 and bronchi 17. A bolus of food, a denture, a pin or a needle are the most common objects found. *Symptoms* will depend upon the size of the object, its exact location, and the amount of secondary irritation and inflammation. *Treatment* is removal of the foreign body and, if necessary, tracheotomy for obstruction. The patient may suffocate before proper medical aid can be instituted.

Trauma.—Trauma to the larynx is closely associated with trauma to the trachea which is considered in the ensuing chapter. Its *causes* are protean and may be conveniently divided into peacetime and wartime injuries. *Peacetime* injuries include suicidal attempts, as for example cuts and compression by hanging, and numerous diversified chance injuries sustained in highway, railroad, industrial and other accidents. In *wartime*, the injury may be due to shrapnel, a bullet or a blow, to inhalation of poisonous gases or to aspiration of intense heat as for example that associated with flame throwers. Consequently, the lesion may consist of a crush, contusion, incision, laceration, puncture, fracture dislocation or scorching of the mucosa. *Symptoms* are due to occlusion of the airway and consist of hemoptysis, cough, hoarseness, difficulty in breathing and cyanosis. The initial *pathologic* changes are of a non inflammatory nature and comprise displacement of tissue, hemorrhage either into the tissues or into the lumen of the larynx and trachea, and submucosal or subcutaneous emphysema. Subsequently, occlusion of the laryngeal lumen results from inflammation and edema and later from cicatricial stenosis. The extent of the injury must always be determined by eliciting a careful history and by local, laryngoscopic and roentgenographic examination. *Treatment* consists of tracheotomy, débridement, rebuilding of the larynx and plastic repair. Immediate *complications* in addition to laryngeal occlusion are pulmonary atelectasis, mediastinal emphysema and rarely pneumonia. Delayed complications as already mentioned are cicatricial stenosis.

The *prognosis* depends upon the extent of the injury. If the cartilage and perichondrium are not injured recovery is good. If they are injured there will almost certainly follow an inflammation, suppuration and necrosis of the cartilages with consequent fibrous stenosis of the larynx. Perforation of the hypopharynx and esophagus is attended by infection, delayed healing and extensive fibrosis.

Laryngeal Obstruction.—Most of the diseases of the larynx which have been considered in this chapter are capable of occluding the laryngeal lumen. Very briefly they may be enumerated under the following four headings: (1) *congenital* such as stridor, web, cyst, hypoplasia or aplasia; (2) *inflammatory* including among others acute infections, edema, and specific granulomas as scleroma, glanders, leprosy, sarcoidosis, tuberculosis, syphilis, and blastomycosis; (3) *tumors*. This comprises any of the benign or malignant neoplasms originating in the larynx and others arising in extrinsic tissues such as thyroid and lymph nodes, and (4) *mechanical* com-

prising laryngeal paralysis, hematoma, foreign bodies and trauma. The latter includes cicatricial stenosis resulting from external injuries as already outlined and from internal injuries in the form of scalds, injudicious use of cautery, intubation tube and tracheotomy.

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Chapter V

TRACHEA, BRONCHI AND LUNGS

EMBRYOLOGY

THE *trachea* and *bronchi* are derived from the proximal portion of the primitive entodermal tube. They are first identifiable in the 3 mm embryo with the appearance of a median laryngo-tracheal groove which gradually deepens and ultimately separates, from below up, the lung buds, bronchi and trachea anteriorly, from the esophagus posteriorly. Subsequently, the trachea elongates and descends caudally. The primitive entodermal lining remains as the epithelium and from this arise the submucosal glands. A differentiation of the surrounding mesenchyme into muscle and cartilage finally completes the formation of the trachea.

The main lung buds bifurcate at the 4 mm stage to form a right and left primary bronchus. The former then forms three subdivisions—an upper apical or eparterial, a middle and a lower whereas the latter forms only an upper and a lower. A lobe of a lung will ultimately form about each of these. Arborization of the peripheral bronchial buds continues in all directions till the sixth month of fetal life, and is again resumed post nally until a total of twenty-four generations is reached. Portions of the median mass of mesenchyme, which cap and are carried laterally by the bifurcating buds, ultimately form muscle, cartilage and connective tissue and into these grow blood vessels and nerves. The visceral pleura comes from the splanchnic mesoderm and the parietal pleura from the somatic mesoderm. Each is covered with mesothelium.

ANATOMY

The *trachea* measures approximately 11 cm. in length and 2.5 cm. in diameter. Its lining mucosa consists of ciliated pseudostratified columnar epithelium wherein are found numerous goblet cells and, along the basement membrane, basal cells (Fig. 126). The submucosa harbors fat, loose connective tissue, elastic fibers, blood vessels, nerves, lymphatics and both serous and mucous glands which open into the lumen by short ducts. External to the submucosa there are 15 to 20 cartilaginous rings whose posterior free ends are joined by transverse bands of smooth muscle. Strong fibro-elastic tissue unites the muscle to the perichondrium and also encircles the trachea externally.

The structure of the extrapulmonary *bronchi* is the same as that of the trachea, but within the lungs the cartilaginous rings are replaced with plates that completely encircle the lumen. Beyond the main bronchi the ramifications consist of secondary bronchi, bronchioles, terminal bronchioles, respiratory bronchioles, alveolar ducts, alveolar sacs and alveoli. As the cartilaginous plates become

irregularly distributed about the lumen interlacing bundles of smooth muscle appear beneath the mucosa and, mixed with elastic bundles, they form a more or less continuous ring that can be traced all the way to the alveolar ducts. As the bronchi ramify certain changes appear in the tubes. Thus submucosal glands disappear after the fifth generation and cartilages after the seventh. The epithelium becomes simple after the eighth bifurcation, loses its cilia after the tenth and becomes cuboidal after the eleventh. The cells lining the *alveoli* are most difficult to visualize and, consequently, this has been a moot subject. There are four current views regarding the nature



FIG 126 —A relatively normal trachea showing a mucosa of ciliated pseudostratified columnar epithelium, a basement membrane, submucosa of connective tissue, a duct, submucosal glands, fat tissue and a piece of cartilage surrounded by fibro-elastic tissue x 100.

of these cells: (1) that they are epithelial and continuous, (2) that they are epithelial and discontinuous, (3) that they are mesenchymal and (4) that they are both epithelial and mesenchymal.

The *lymph vessels* of the lungs consist of one system beneath the pleura which ultimately empties into the broncho-pulmonary nodes, and another system which follows the branches of the pulmonary vessels and bronchi deep in the lung and empties into the tracheo-bronchial nodes. The lymph vessels of the parietal pleura drain into the sternal, diaphragmatic and posterior mediastinal nodes. The right and left bronchomediastinal trunks drain the corresponding tracheobronchial and other mediastinal nodes and enter the respective junctions of the internal jugular and subclavian veins.

TRACHEA

PATHOLOGY

Congenital Anomalies—Important congenital abnormalities of the trachea are fortunately quite rare. There have been described aberrant bronchi which arise in the lower third of the trachea and on the right side, stenosis which may or may not be congruous with life, atresia or complete absence of the lower portion of the trachea which, of course, is always fatal, and, more commonly, *tracheoesophageal fistula* and *diverticulum*.

Tracheoesophageal Fistula—This is perhaps the most common abnormality. The opening is always found in the lower portion of the trachea 0.5 to 1.0 cm. above the bifurcation and is due to a failure of fusion of the lips of the laryngotracheal groove. The trachea opens most frequently into the lower segment of the esophagus and only rarely does it also communicate with the upper segment which usually ends as a blind sac. Because of these associated abnormalities, regurgitated food from the upper pouch of the esophagus or from the stomach (in cases in which a gastrostomy has been performed) finds its way into the trachea and produces attacks of choking, dyspnea and cyanosis. The end result is a fatal pneumonia unless the fistula is repaired. The anomaly is considered in more detail under congenital abnormalities of the esophagus.

Tracheal Diverticulum—Another anomaly that is being recognized more frequently is a diverticulum of the trachea. This lesion has been described under several names some of which are *teroceles*, *tracheoceles*, *tracheaectasis*, *tracheal hernia*, *aerial goiter* and *bronchocele*. It consists of a herniation of the mucosa of the trachea between the muscle fibers of its posterior portion and is usually located on the right side. The ostium may be so small that it cannot be found at all or it may be as large as the diverticulum itself. The number of diverticula in a single case varies from one to many and the size from 6 mm. to 5 cm. or more. The *genesis* is in doubt, but it is probable that some are *congenital* while others are *acquired*. Advocates of the former theory point to the fact that they occur in the same location as do accessory bronchi, and advocates of the latter theory hold that the areas between the muscle bundles in the posterior wall are weak spots that give way during increased intratracheal pressure. Infection and breakdown of submucosal glands is another factor that allegedly contributes to the mural weakness. At any rate the condition is *usually asymptomatic*, although choking, coughing, wheezing and dyspnea have been described. Physical examination may show a soft reducible swelling usually on the right side of the neck, a simple roentgenogram will disclose an air filled pocket, a barium filled esophagus will be displaced to the left and posteriorly (when the diverticulum is large), and a tracheoscopy may reveal both the ostium and the sac. *Treatment* has been unnecessary. A lesion closely allied to a tracheal diverticulum is a bronchial cyst which will be considered under cysts of the mediastinum.

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Inflammation.—Inflammatory lesions of the trachea fall into the realm of surgical pathology only when they produce obstruction to the airway.

Acute Mucopurulent Tracheitis.—This is always associated with a similar process in the bronchi. In adults it is of little significance unless the airway is previously partly occluded but in infants it may of itself cause death by suffocation. (I have performed autopsies on two such cases within the last year.) The tracheal lesion is usually preceded by a laryngitis which leads to obstruction and necessitates a tracheotomy. Obstructive *symptoms* are then temporarily alleviated only to return with increased severity. At

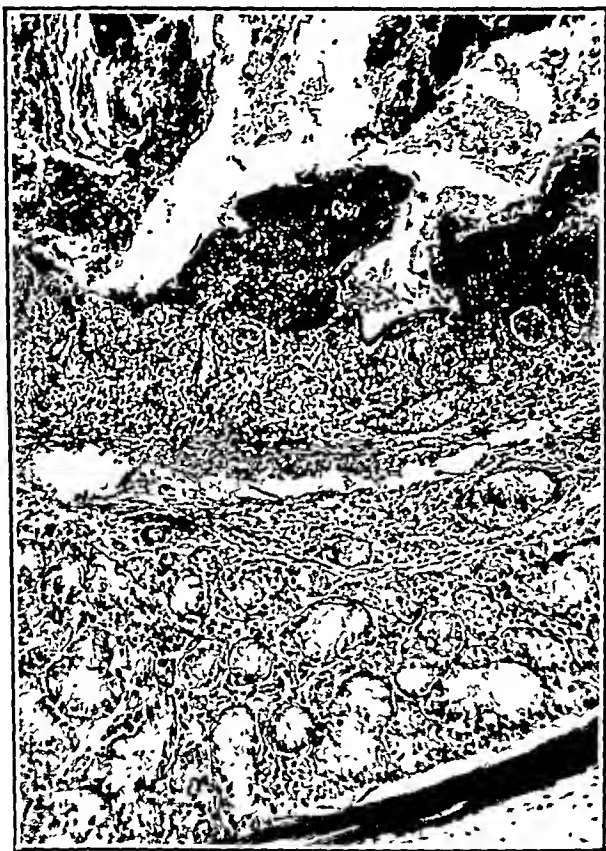


FIG 127.—Acute mucopurulent tracheitis in an infant. The lumen is filled with tenacious pus, the epithelium has sloughed, the submucosal glands are distended with secretion and the submucosa is infiltrated with leukocytes x 75.

autopsy the lower portion of the trachea and the main bronchi are completely filled with a sticky, tenacious, mucopurulent secretion. The mucosa is superficially ulcerated and both it and the submucosa are reddened, thickened and edematous. The lungs show alternating areas of emphysema and atelectasis. *Histologically*, the mucosal epithelium is at first vacuolated and then denuded and the submucosa reveals engorgement of the capillaries, edema of the supporting connective tissue, a diffuse infiltration with neutrophils and fewer numbers of plasma cells and lymphocytes, and a distension of the glands and their ducts with mucus (Fig. 127). Culture of the secretions yields a growth of organisms usually found in the respiratory tract with one of the streptococci predominating.

Chronic Non-specific Tracheitis—The only lesion of surgical importance in this category is the non-specific inflammation that accompanies intensive *roentgen therapy* to the neck. The larynx is usually affected more severely than the trachea but sometimes it entirely escapes injury and the trachea alone is involved. Depending upon the degree of irradiation, there may or may not be hyperemia and edema of the mucosa and submucosa in the early stages. The end result, however, is a cicatricial stenosis of the lumen of the trachea. The normal structures including the muscle and even cartilage are gradually replaced with dense, acellular and avascular fibrous tissue. Of particular gravity are the cases exhibiting perichondritis for this leads to extensive necrosis and



FIG. 128—Blastomycosis of the trachea. There is metaplasia of the mucosa to stratified squamous epithelium, fibrosis of the submucosa, a diffuse infiltration with plasma cells, monocytes and other leukocytes, and metaplasia of a tracheal cartilage to bone. $\times 375$

sequestration of the cartilaginous rings resulting in collapse of the wall and complete stenosis of the lumen.

Chronic Specific Tracheitis—Only four granulomatous lesions of the trachea need be mentioned.

Tuberculosis—With the exception of those cases in which infected lymph nodes break through the wall, tuberculosis of the trachea is always secondary to tuberculosis of the lungs and bronchi. The lesion is the same as that in the bronchi which is considered in the section on tuberculosis of the lung (p. 175).

Scleroma—This usually involves the nasopharynx and the larynx, but sometimes it descends into the trachea where it will

produce obstruction. The condition has been considered in detail in the chapter on the upper respiratory system (p. 117).

Blastomycosis.—Blastomycosis of the trachea is sometimes found as an extension of the lesion from the larynx. In a case that recently came to necropsy the disease started in the larynx fourteen years previously at which time a tracheotomy was performed because of laryngeal obstruction. In this interval the original lesion healed with extensive fibrosis and distortion of the larynx, but the disease extended inferiorly to involve the entire trachea, main bronchi and their immediate subdivisions. The lumen of the trachea was reduced to a narrow verticle slit and was filled with secretion. The mucosa was grey, tough and thick and the submucosa was prominent and fibrotic. All the cartilages of the trachea and bronchi were at least partly calcified or ossified. Both lungs revealed extensive bronchiectasis and numerous abscesses. *Histologic* sections of trachea and bronchi disclosed (1) a mucosa of hypertrophied stratified squamous epithelium, (2) extensive fibrosis of the submucosa with a diffuse infiltration with plasma cells, lymphocytes and fewer neutrophils together with focal collections of mononuclear cells and giant cells that occasionally contained spores and (3) in the areas of ossification, adult bone and bone marrow (Fig. 128).

Syphilis.—Syphilis of the trachea is not common. *Secondary* lesions like in the mucosa of the mouth may consist of papules or shallow ulcers. *Tertiary* lesions are either of a diffuse granulomatous type or of the gummatous variety. The latter are numerous and small, or few and large with a tendency to early ulceration. *Histologically*, they are similar to the tertiary lesions already described in the skin.

Tumors.—Neither benign nor malignant tumors of the trachea are common. Those that have been described are: from the mucosa a papilloma and carcinoma; from submucosal glands an adenoma; from connective tissue a fibroma, amyloid tumor and fibrosarcoma; from blood vessels an angioma and hemangioendothelioma; from fat tissue a lipoma; from lymphoid tissue a lymphoma; from the perichondrium an osteoma; from congenitally misplaced thyroid tissue a goiter, and from distant areas metastatic tumors. Most of these are self-explanatory and will not be considered further. Adenoma of the trachea is similar to adenoma of the bronchus which is described under tumors of the lungs. Osteoma, carcinoma, sarcoma and metastatic growths are common enough to merit some discussion.

Tracheopathia Osteoplastica.—This cumbersome name has been applied to multiple bony tumors of the trachea. They are not common and until recently most of the reported cases have been diagnosed at autopsy but, with the advent of bronchoscopy, more and more are being discovered during life. The *symptoms* consist of gradually increasing dyspnea, hoarseness, cough, expectoration and hemoptysis. Small nodulations of osseous tissue first appear under the mucosa and between the cartilaginous rings of at least the lower two-thirds of the trachea and the main bronchi. The membranous portion of the trachea, however, is not affected. These

nodules gradually increase in size and number until they produce severe narrowing of the airway. *Histologically*, the tumors are composed of adult bone containing fully developed marrow (Fig. 129). They have been considered to arise as (1) an exostosis, (2) a congenital anomaly of the perichondrial connective tissue, (3) an alteration of the elastic tissue elements and (4) a transformation of connective tissue. An origin from the perichondrium of the tracheal and bronchial cartilages or an ossification of the cartilages themselves seems to be the most logical explanation, first, because bone formation is very commonly seen in the cartilaginous rings as an incidental finding at necropsy, and second, because the tumors are found only in the vicinity of the cartilages and not in the membra-



FIG. 129—Osteoma of the trachea shown, adult bone in the submucosa. The mucosa is composed of stratified squamous epithelium. $\times 300$

nous portion of the trachea. *Treatment* is most difficult and the ultimate *prognosis* is not good.

Carcinoma—Carcinoma of the trachea is about five times as common as sarcoma. The age limits are eighteen to eighty-two years with 90 per cent occurring between the ages of thirty and seventy years. Men are affected twice as frequently as women. The earliest *symptom* is a tickling sensation in the trachea and this is followed later by an irritating cough, persistent hoarseness, constant or paroxysmal dyspnea brought about by change in position, hemoptysis, wheezing respirations and asphyxia.

The tumor usually originates in the membranous portion of the trachea and the level in order of frequency is the lower third, upper third and middle third. Ordinarily, the neoplasms are localized, flat, infiltrating, polypoid or pedunculated but occasionally they are

annular and both surround and constrict the entire lumen. They all tend to penetrate the wall of the trachea and extend into the esophagus. About 70 per cent *metastasize* to the mediastinal, peribronchial and cervical lymph nodes and less often to the lungs, bones, gastrointestinal tract, liver, pancreas, spleen and kidneys.

The literature regarding both the *histogenesis* and the microscopic classification is confused. Theoretically, carcinoma of the trachea may arise in the mucosa and the submucosal glands and ducts. It is probable, however, that most of the tumors originate in the surface epithelium. The basal cells of the mucosa of the trachea like those of the bronchi are primitive cells that normally differentiate into goblet, cuboidal and columnar cells. Therefore, they should be capable of producing a tumor composed entirely of any one of these cells in which case the arrangement would be of an acinous or adenomatous type. When irritated the basal cells also produce stratified squamous epithelium and, therefore, when they undergo neoplasia there is no reason why they cannot produce a squamous cell carcinoma. The submucosal glands and their ducts, on the other hand, are similar to the submucosal glands of the mouth and even to the salivary and parotid glands and when each undergoes tumefaction the neoplasm is usually a benign adenoma. At times, however, the submucosal glands of the trachea may form an adenocarcinoma, although this is probably as infrequent as the development of an adenocarcinoma in a submaxillary gland. At any rate it is generally agreed that there are two *histologic types* of carcinoma, namely, an adenocarcinoma and a squamous cell carcinoma. Each of these is highly malignant—the patients usually dying within a year. Hence, reports in the literature of adenocarcinoma of the trachea cured by simple excision, irradiation or both should be regarded with skepticism. It is probable that most if not all of these cases are variants of benign adenoma. It is also likely that the so-called cylindroma (cylinders of connective tissue interspersed with strands of tumor) of the trachea also falls into this category. Both of these will be considered further under adenoma of the lung.

The *diagnosis* of the carcinoma of the trachea is made from a consideration of the history, the roentgenograms including tomography, direct laryngoscopy, tracheoscopy and most important a biopsy. *Treatment* is most unsatisfactory. It consists of surgical excision of the tumor area, destruction of the tumor by electrocoagulation, implantation of radium and roentgen-ray irradiation. The *prognosis* is grave.

Sarcoma.—Sarcoma of the trachea occurs in a somewhat younger age group than does carcinoma. Like other tumors in this region they gradually occlude the lumen. The most common single *symptom* is inspiratory and expiratory stridor. Many of these tumors are said to develop from an originally benign fibroma and, therefore, they grow rather slowly. The most common location is the upper portion of the trachea with an origin from the posterior or lateral wall. Usually they are attached by a broad base but sometimes they are polypoid. *Histologically*, most of them are composed of spindle or round cells with scanty cytoplasm although some are

definitely myxomatous. The latter are said to arise from submucosal mixed tumors of the salivary gland type. The *treatment* and *prognosis* parallels that of carcinoma of the trachea.

Secondary growths of the trachea are much more common than are primary lesions. Any tumor that grows in the vicinity of the trachea may compress or penetrate its wall. Primary carcinoma of the thyroid gland and of the esophagus, lymphoblastomas particularly Hodgkin's disease, thymoma and mediastinal teratoma are the most common offenders. Of the metastatic cancers to the neighboring lymph nodes that cause tracheal compression carcinoma of the lung leads the list.

Mechanical Disturbances—Foreign Bodies—Once a foreign body passes the larynx its chances of lodging in the trachea are relatively small. In a consecutive series of 413 foreign bodies in the air passages, Clerf found 19 in the larynx, 37 in the trachea and 337 in the bronchi. The subject is considered in greater detail in the section on the lungs.

Trauma—The most common injuries to the trachea result from cuts, bullets and blows. The former two usually produce a direct communication with the exterior resulting in a rush of air, bloody froth, dyspnea, cyanosis and cough. The latter produces a subcutaneous rupture with rapidly ensuing emphysema into the soft tissues. In one or two hours this may extend from the eyes to the scrotum. There are in addition ecchymosis and edema into the soft tissues of the neck.

Symptoms consist of pain, dyspnea, cough, cyanosis, wheezing, hoarseness and bloody mucoid expectoration. The principal consideration in the treatment of these cases is the maintenance of an adequate airway. The prognosis is good.

Tracheotomy—Tracheotomy is performed to relieve obstructive symptoms usually produced by lesions in the larynx and sometimes to aid in ridding the tracheobronchial tree of excessive secretions particularly in cases of foreign bodies in the air passages. Four complications that may follow tracheotomy are (1) subcutaneous emphysema, (2) tension pneumothorax, (3) cellulitis of the neck about the ostium and (4) cicatricial stenosis of the trachea. The most frequent and least important is subcutaneous emphysema, and the most serious is tension pneumothorax. The latter will be considered in the section on the pleura (p. 204).

Tracheal Obstruction—Obstruction to the trachea can be produced by almost all of the aforementioned diseases. In general it may be caused by factors (1) within the lumen, (2) within the wall and (3) pressure from the outside. Foreign bodies are the only important objects that are found free *within the lumen*. Diseases of the *wall* itself cause obstruction by producing a uniform thickening of the wall and corresponding narrowing of the lumen or by means of pedunculated or sessile masses projecting from the wall. Among the lesions in this category may be mentioned congenital stenosis, acute and chronic inflammations, benign and malignant tumors, traumatic edema and hemorrhage, and cicatricial stenosis resulting from tracheotomy, excessive irradiation, inhalation of gases, in-

flammation and direct trauma. Lesions producing *compression* of the trachea from without may be divided into those in the neck and those in the mediastinum. The former includes diseases of the thyroid both inflammatory and neoplastic, diseases of the cervical lymph nodes particularly the lymphoblastomas and metastatic carcinoma, and carcinoma of the esophagus. Some of these also operate in the mediastinum but in addition there are congenital anomalies of the larger vessels (such as a double aortic arch), aneurysm of the aorta, thymoma, teratoma, and other tumors and cysts primary of this region.

BRONCHI AND LUNGS

PATHOLOGY

Congenital Anomalies.—Congenital abnormalities of the bronchi and lungs are quite common although they frequently produce no symptoms until adult life is reached. They will be considered under the following four headings: (1) accessory and aberrant bronchi and lung, (2) agenesis of the lung, (3) cystic disease of the lung and (4) situs inversus.

Accessory and Aberrant Bronchi and Lung.—The level of the bifurcation of the main *bronchi* may vary resulting in a *shorter* or *longer* main stem in some individuals as compared with others. This is obviously of considerable practical importance for short bronchi may offer the surgeon considerable difficulty in completely extirpating a primary bronchogenic carcinoma. *Extra* bronchi are not too common. As already mentioned an *accessory* bronchus usually arises from the lower portion of the trachea on the right side but sometimes it is seen on the left. *Congenital obstruction* to a main bronchus is infrequent and may consist of a membranous diaphragm that completely spans the lumen or a maldevelopment of the pulmonary veins that compresses the wall from the outside.

One of the most frequent and least important anomalies is the *number* of major lobes. There may be two on the right side instead of the customary three, and three on the left side instead of two. Of more significance are *accessory* or supernumerary lobes. Sometimes these are connected by aberrant bronchi to the main airway and then function as ordinary lung tissue, but at other times such a communication is lacking and the mass is physiologically inert. There are three common *sites* for *accessory lung* tissue. The *first* is the apex of the right lung where a deep cleft of pleura containing the azygos vein partially pinches off a piece of lung parenchyma to form the "azygos lobe." The significance of this is threefold: (1) it often produces an aberrant shadow on a roentgenogram and although it is undiseased it may be mistaken for apical tuberculosis, (2) it may actually be the seat of a tuberculous or other infection and (3) it may cause the surgeon considerable mechanical difficulty at the time of a pneumonectomy. A *second* location for accessory lung tissue is high in the mediastinum and lateral to the trachea

where it constitutes a "tracheal accessory lung." This usually communicates with the trachea by a separate bronchus. A third common site for aberrant lung tissue is the inferior portion of the left side of the chest between the lower lobe of the lung and the diaphragm. It is attached to the lung, mediastinum, diaphragm or even stomach and is always covered with pleura, but it has no communication with the tracheobronchial tree. Its blood supply comes from the thoracic aorta and it is composed of dilated but otherwise quite regular bronchial radicles. Although it arises from entoderm, the question is does it originate directly from the primitive foregut or from the lung proper? It is important (1) because it may undergo complete degeneration with increase in size to produce an epithelial lined cyst and (2) because it may become infected by way of the blood or lymph stream and produce disturbances such as are consequent to any localized pulmonary infection.

Agenesis of the Lung—Congenital absence of a lung is probably more frequent than the scanty reports in the literature tend to indicate. It occurs twice as often on the left side as on the right, and in three males to every two females. Two-thirds of the cases have been recognized in children under twelve years. The symptoms are inconsistent or entirely lacking but when present they consist of dyspnea, stridor and cyanosis. Examination discloses an absence of the usual physical findings on the affected side. Five theories have been advanced to explain the cause of the agenesis: (1) atavistic reversion to a reptilian stage, (2) abnormal pressures on the fetus in utero, (3) phylogenetic newness associated with the enormous growth of the lung, (4) infection in utero and (5) some inherent defect in the germ plasma itself. The latter is probably the correct explanation for there are often other associated local and distant anomalies.

As seen from the embryology, the condition is an arrest of development of a lung and the stage at which the arrest occurs will determine the amount of pulmonary tissue present. There may be (1) no trace of a lung, lung bud, bronchus or vascular supply to the affected side. In such cases the trachea and remaining bronchus form a continuous straight tube without any narrowing or much angulation, (2) a small outpocketing of the trachea where the bronchus should be with no surrounding pulmonary tissue and (3) severe hypoplasia where the bronchus is fairly well developed, reduced in size and surrounded by a mass of underdeveloped, unlobulated lung parenchyma. The affected pleural cavity is filled with fluid or displaced mediastinal structures particularly heart and thymus. Associated local anomalies that have been described consist of a defective or absent pleura, narrowing of the trachea, increase in number of tracheal cartilages, tracheoesophageal fistula, absence of pulmonary vessels to the affected lung, a common trunk for the main aortic vessels, and in the remaining lung hypertrophy, emphysema, abnormal lobulation and bronchiectasis. Other defects that have been noted are synostosis of the ribs, absence of the diaphragm, atresia of the anus, hare lip and cleft palate and abnormalities of the extremities.

The *diagnosis* is suspected in the absence of the usual physical signs and roentgenographic markings on the affected side, and is confirmed by a bronchoscopic examination and a bronchogram. Without resort to the latter two, agenesis of the lung may be confused with pneumonia, massive atelectasis, foreign body in a bronchus, hydrothorax, diaphragmatic hernia and paralysis of the diaphragm. The *prognosis* is guarded (1) because other associated and more serious anomalies may be present, and (2) because having only one functioning lung any normally insignificant pulmonary lesion on the good side may cause death. Only 20 per cent of the reported cases have lived beyond the age of nineteen years, and 3 have reached the ages of fifty-eight, sixty-five and seventy-two years.

Cystic Disease of the Lung.—Cystic disease of the lung has been described under *many names* some of which are honey-combed lung; cystic, fetal, congenital or atelectatic bronchiectasis; true congenital cysts; congenital pulmonary lymphangiectasis; pneumatocele; pneumocyst; chronic interstitial, chronic bullous or progressive bilateral bullous emphysema, and vanishing lung. Although there has been considerable controversy regarding the *genesis* of pulmonary cysts it is, at the present time, generally conceded that some are *congenital* whereas others are *acquired*. For the sake of convenience both forms will be considered here.

Congenital Cysts.—Despite the fact that this anomaly is developmental in origin the disease is not always recognized at birth. Roughly one-quarter of the cases have been found from birth to one year of age, another quarter between the ages of one and fifteen years, and the rest over fifteen years. *Symptoms* are usually absent until (1) the cyst becomes progressively distended with air when there will be recurring attacks of cyanosis, dyspnea and cough, and (2) the cyst becomes infected by way of an opening into a bronchus when there will be cough, expectoration of sputum, fever, anorexia, weight loss, pains in the chest and other signs and symptoms associated with bronchiectasis. Hemoptysis to as much as 500 cc. at a time occurs in about 13 per cent of the cases.

The *lesion* is a congenital malformation which may *arise* early or relatively late in the development of the lungs by a pinching off of portions of the main lung buds or their derivatives. If the arrest is early, a globular solitary cyst will form from an accessory bronchial bud and it will be situated between the pulmonary lobes or project in front of or behind the lung roots. If the arrest is later, numerous smaller cysts will form from the more peripheral bronchi and bronchioles and these will be scattered throughout the lung parenchyma. The exact mechanism involved in the formation of congenital pulmonary cysts is unknown but it is generally ascribed to two factors (1) a pull by the normally faster growing thoracic cage on the underdeveloped bronchopulmonary segment resulting in its cystic dilatation, and (2) accumulation of fluid secreted by the epithelial cells lining the affected bronchioles. This causes a distention of the undeveloped segment with the formation of a cyst. Subsequently, the fluid ruptures into a bronchus and is replaced with entrapped air which in turn causes a further increase in size.

As already indicated the *cysts* may be single or multiple, large enough to occupy an entire hemithorax or only a few millimeters in diameter, and they may be situated at the hilum or in any part of the lung. Usually the disease is limited to one side, but occasionally it is bilateral. At birth the cysts contain milky or turbid fluid which, however, is soon replaced with air if a communication exists with a bronchus. Unless infected the lining is always smooth, glistening, grey and, in the solitary ones, trabeculated (Fig 130).



FIG 130

FIG 131

FIG 130—Congenital cyst of a lung. The lining is smooth and trabeculated. An applicator indicates one of six communications with bronchi that were demonstrated in this specimen.

FIG 131—Wall of congenital cyst shown in figure 130. The lining is composed of ciliated pseudostratified columnar epithelium and the submucosa is infiltrated with plasma cells and lymphocytes. $\times 200$

When infected the larger cysts appear like ordinary abscesses and the smaller ones are indistinguishable from acquired bronchiectasis. Communications with bronchi are free, direct and easily demonstrable in the multiple variety, but they enter the wall obliquely and are sometimes difficult to find in the solitary ones. Histologically, the former closely duplicate the structure of a bronchus in that their walls consistently disclose ciliated, cuboidal or columnar epithelium, a basement membrane, smooth muscle, mucous glands and cartilage. The larger cysts are similar except that the smooth muscle, mucous glands and cartilage are less abundant and more irregularly distributed (Fig 131).

The condition may be suspected from the clinical signs and symptoms but often it is asymptomatic and is discovered accidentally. An ordinary roentgenogram of the chest reveals circumscribed areas of decreased density. A bronchogram shows cystic dilatations of the terminal portions of the bronchial tree in cases with multiple cysts and, as a rule, a complete filling defect of the airway in the involved area of a single cyst, with, at the same time, a peripheral crowding of the adjacent bronchi. Increased tension in the cyst may be released (1) spontaneously by a rupture into the pleural cavity, in which case the rent soon heals, and the episode is repeated (2) by needle aspiration through the chest wall with also only temporary relief, (3) by trocar and catheter insertion through the chest wall for more prolonged aspiration and (4) by marsupialization of the cyst onto the chest wall. The most effective *treatment*, however, is complete enucleation of the cyst, lobectomy or pneumonectomy. The *mortality* is high in infants and children but the prognosis in adults is considerably better. Death is due to the cystic disease itself, to pneumonia, to tuberculosis, or to right sided heart failure.

Acquired Cysts.—Usually acquired cystic disease is associated with respiratory infection, chronic bronchitis, peribronchitis, pulmonary fibrosis or bronchial asthma. These produce incomplete bronchial obstruction which is followed by overdistention of the corresponding alveoli, rupture of the walls and the formation of blebs and bullae which also coalesce until large portions of the lung are replaced with air sacs. Sometimes, however, the same sequence of events takes place without any demonstrable bronchial occlusion. In such instances the dissolution of the lung is apical, bilateral and progressive until ultimately most or all of the lung is converted into cyst-like spaces. So far this bilateral progressive lesion has been described only in men in the third and fourth decades of life. The *symptoms* are cough, increasing dyspnea, recurring infections of the respiratory tract, asthma-like attacks and cachexia. *At autopsy* one finds thin, cyst-like emphysematous bullae of varying sizes replacing most of the lung and crowding the remaining portions. *Histologically*, the sac wall is composed of compressed, pulmonary parenchyma that usually contains carbon pigment. There is no epithelial lining. The *diagnosis* is made from roentgenograms of the chest which, in the early stages, disclose a replacement of the normal apical markings by a patternless tracing of fine linear shadows and later by definite cyst-like spaces compressing the lower lobes. Bronchography reveals a depression of the bronchi of the upper lobes by the bullae. There is no effective *treatment*. The *prognosis* is poor, none of the cases having lived longer than eight years after symptoms became manifest. *Death* ensues when there is insufficient pulmonary tissue left to carry on normal respiratory exchange.

Situs Inversus.—Situs inversus is a mirror image transposition of all the thoracic and abdominal organs. The heart projects into the right pleural cavity; the aortic arch is on the right side; the right lung has two lobes, and the left lung has three. It is mentioned here because many of the cases are also accompanied by an

absence or infection of the paranasal sinuses and by bronchiectasis. This combination of anomalies has been referred to as *Katagener's triad*. Although the malformation is present at birth it is frequently not recognized until adult life is reached and the *symptoms* then are those consequent to the bronchiectasis. Sinusitis is suspected from the history, and both it and the absence of some of the sinuses are discovered in routine roentgenograms. Transposition of the thoracic viscera is demonstrated by ordinary roentgenography of the chest, transposition of the colon by barium enema and bronchiectasis by bronchogram. The frequent association of this group of anomalies favors the hypothesis that some cases of bronchiectasis are of congenital origin.

Inflammation—There are four inflammatory conditions of the the bronchi and lungs that are of surgical importance: (1) bronchiectasis, (2) abscess, (3) tuberculosis and (4) lipid pneumonia.

Bronchiectasis—The term bronchiectasis, as used today, signifies infection and dilatation of the bronchi. It is a common disease which usually starts in childhood, and affects both sexes with equal frequency. Early in its course it produces no characteristic *symptoms* and the condition is often uncovered in a routine examination. In children it usually starts as an acute pulmonary process with chills and fever, to be followed in a few days by a dry hacking cough, and later by expectoration of mucoid material. Recurring attacks of "bronchitis" and "pneumonia" are frequent until in the advanced stages there is a severe, hacking and persistent cough with expectoration of abundant, foul-smelling, often blood-streaked sputum. Fever is present when drainage is inadequate.

Theories regarding the *pathogenesis* of bronchiectasis have been rampant but only a few of them need be considered here. This is perhaps best accomplished by dividing the cases into the following three groups: (1) congenital, (2) primary of uncertain etiology and (3) secondary to known cause. Little more need be said about cases of *congenital* origin as this has already been alluded to in the discussion of congenital cystic disease of the lung. The best evidence perhaps that the disease can originate as a developmental anomaly is the frequency with which it is associated with other congenital malformations, particularly, situs inversus and fibrocystic disease of the pancreas. The number of cases in this category, however, as compared with those in the other two is probably exceedingly small.

Most of the cases, especially in children, are to be found in the second group—*primary of uncertain etiology*. The onset of the disease is almost always dated from an illness such as pneumonia, pertussis, scarlet fever, measles, influenza, immersion, empyema or diphtheria. The role which each or any of these plays in the development of bronchiectasis has been a moot question, but in light of Anspach's recent work they can no longer be passed off as entirely incidental. He carefully studied a group of 50 children from the clinical, roentgenologic and pathologic standpoints, and concluded that the sequence of events is as follows. Bronchial secretion, whether initiated by inflammation or aspirated foreign material,

The condition may be suspected from the clinical signs and symptoms but often it is asymptomatic and is discovered accidentally. An ordinary roentgenogram of the chest reveals circumscribed areas of decreased density. A bronchogram shows cystic dilatations of the terminal portions of the bronchial tree in cases with multiple cysts and, as a rule, a complete filling defect of the airway in the involved area of a single cyst, with, at the same time, a peripheral crowding of the adjacent bronchi. Increased tension in the cyst may be released (1) spontaneously by a rupture into the pleural cavity, in which case the rent soon heals, and the episode is repeated (2) by needle aspiration through the chest wall with also only temporary relief, (3) by trocar and catheter insertion through the chest wall for more prolonged aspiration and (4) by marsupialization of the cyst onto the chest wall. The most effective *treatment*, however, is complete enucleation of the cyst, lobectomy or pneumonectomy. The *mortality* is high in infants and children but the prognosis in adults is considerably better. Death is due to the cystic disease itself, to pneumonia, to tuberculosis, or to right sided heart failure.

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Situs Inversus.—Situs inversus is a mirror image transposition of all the thoracic and abdominal organs. The heart projects into the right pleural cavity; the aortic arch is on the right side; the right lung has two lobes, and the left lung has three. It is mentioned here because many of the cases are also accompanied by an

dull, granular and necrotic. A prominent feature is a transverse trabeculation of the mucosa. At this stage the bronchial walls are thick, grey and rigid. The intervening lung tissue is grey, firm, non-crepitant and frequently contains abscesses. The visceral and parietal pleuras are closely bound together by dense, fibrous adhesions.

The earliest *microscopic* changes are indistinguishable from bronchopneumonia. The lumen is filled with neutrophils, fibrin and debris, the epithelium is partly or wholly denuded, and the wall is infiltrated with neutrophils and a few plasma cells and lymphocytes.

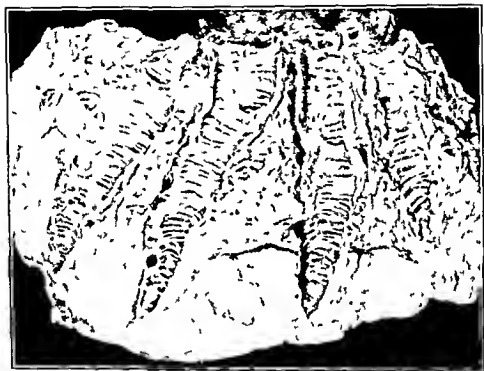


FIG. 132.—Bronchiectasis. The bronchi are uniformly dilated and their walls are transversely trabeculated.

The mural infiltration gradually increases in severity and destroys not only the elastic and muscle tissue but even the cartilages. The result is a weakening of the wall and dilatation. The adjacent parenchyma also participates in the inflammatory process in the form of an exudative or proliferative interstitial pneumonia. Healing begins rather early and is characterized by (1) regeneration of the bronchial epithelium usually to a stratified squamous, but sometimes to a transitional or even a ciliated pseudo-columnar type (Fig. 133), (2) a replacement of the necrotic areas and exudate by granulation tissue which in time loses its overabundance of capillaries and leaves in its stead fibrous tissue, (3) a hypertrophy of the mucous glands, (4) calcification and bone metaplasia of the bronchial cartilages, (5) fibrous thickening of the alveolar septa (Fig. 134), (6) lining of the alveoli with a single layer of cuboidal cells which are often con-

occludes the bronchus. The air distal to the obstruction is absorbed resulting in atelectasis. If this is not relieved by postural or bronchoscopic drainage the consequent inflammation weakens the bronchial wall. The decreased intrathoracic volume as a result of the atelectasis increases the negative intrapleural pressure over the normal and this causes the weakened bronchial walls to dilate. This seems to be the most plausible explanation and fits in not only with cases of ordinary pneumonia but also with pertussis, influenza and others listed above. If Anspach's interpretation is correct then perhaps there is no room for this second category—primary of uncertain etiology.

The third group—*secondary to known causes*—comprises those cases wherein the lumen of the bronchus or bronchi is obviously occluded. The *obstruction* is brought about by (1) foreign bodies in the lumen which are exogenous or endogenous such as caseating lymph nodes, or broncholiths (2) changes in the wall which include congenital stenosis, inflammation either non-specific or specific as tuberculosis are rarely syphilis, tumors both malignant and benign, and cicatricial stenosis consequent to trauma and (3) lesions outside of the bronchus compressing the wall from without. These are due to post pneumonic fibrosis, inflammatory changes in the lymph nodes particularly anthracosilicosis and tuberculosis, primary or secondary extrabronchial tumors, adhesions, pleural effusions and deformities of the thoracic cage such as marked kyphosis and scoliosis.

The question of *paranasal sinusitis* as related to *bronchiectasis* has purposely been omitted from the above tabulation. It is one that has been discussed for years and is no nearer solution now than it was when the controversy first started. In a correlation of the histopathologic changes in the mucosa of the nose and sinuses with those of the trachea, bronchi and lungs, my experience in some 500 cases has been that in acute infections such as pneumococcic pneumonia the intensity and quality of the lesion in one parallels that of the other. The same is true for bronchial asthma but it does not hold for tuberculosis, pulmonary abscess or bronchiectasis where the intensity of sinus infection never begins to approach that present in the lungs. But this proves nothing for pus from sinusitis may have plugged the bronchi and initiated the suppuration in childhood and while the latter becomes progressively worse the former may regress completely.

Bronchiectasis is more often unilateral than bilateral, affects the lower lobes more frequently than the upper and is found as often on the right side as on the left. In the early stages there are no grossly characteristic changes in the lungs. Atelectasis is prominent. The bronchi are plugged with unusually thick secretion and in the surrounding tissue there are small areas of pneumonic consolidation. Bronchial dilatation begins in about three weeks and from this time on it becomes progressively more severe. In the fully developed cases the expansions become cylindrical, sacculated or terminally bulbous (Fig. 132). They vary in size from equivocal enlargements to 3 or 4 cm. in diameter. The lumen is filled with pus and the inner surface of the wall is either smooth and glistening or

Abscess—Lung abscess is not as common as bronchiectasis. It is usually seen in adults thirty to fifty years of age and is twice as frequent in men as it is in women. The usual *symptoms* in order of frequency are cough, pain in the chest, fever, hemoptysis, chills, expectoration of foul-smelling sputum, loss of weight and dyspnea. The disease usually follows pneumonia, tonsillectomy, other surgery, influenza, aspiration of foreign bodies, septicemia, thrombophlebitis, and, rarely, penetrating wounds of the chest. The organisms, therefore, reach the lung (1) by penetration from the outside, (2) by way of the blood stream and (3) by aspiration through the tracheobronchial tree. The first route, even in war, is uncommon and the

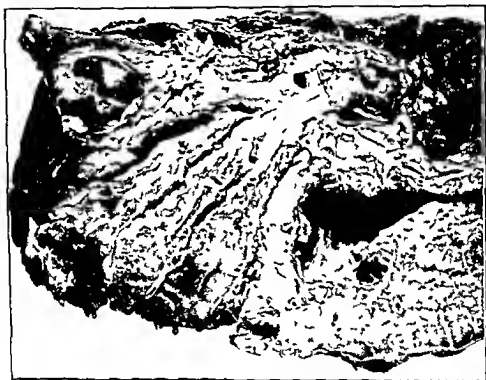


FIG. 130.—Lung abscess. There are two large, smooth-walled cavities that communicated with the bronchi and a third small, more recent peripheral one with a ragged wall. The surrounding tissue shows extensive pneumonia.

second while more frequent still accounts for only a few cases of pulmonary abscess. In such instances the lesions are usually multiple and are found not only in the lungs but also in other organs. Most often they arise as a sequel to staphylococci aureus septicemia, but sometimes they originate in emboli from septic thrombophlebitis or in septic pulmonary infarcts. The former constitutes almost a unique group for staphylococci infections respond to penicillin therapy and surgical drainage is seldom if ever necessary.

Undoubtedly the most common cause of pulmonary abscess is aspiration of septic material into the tracheobronchial tree. Blood clot, viscid mucus, tartar from the teeth, extraneous foreign bodies and pieces of tonsil charged with anaerobic organisms may be the

tinuous with the bronchiolar epithelium, (7) filling of the alveolar spaces with phagocytes containing ingested iodized oil that was used for bronchography and (8) an organization of the intra-alveolar exudate with the formation of granulomatous nodules that have been termed "Masson bodies."

Cultures of pus from the bronchi yield a mixture of pneumococci, streptococci, staphylococci and many other non-specific organisms.



FIG 133

FIG 134.

FIG 133.—Bronchiectasis showing a greatly dilated bronchiole. The mucosa is composed of regular epithelium on the right, is ulcerated in the center and is stratified squamous on the left side. The submucosa is greatly thickened and is infiltrated with leukocytes x 50

FIG. 134.—Bronchiectasis showing extensive interstitial pneumonia and several "Masson bodies" x 75

The *complications* of bronchiectasis are (1) pulmonary abscess, (2) empyema, (3) bronchopulmonary fistula, (4) brain abscess, (5) clubbing of the fingers and toes and (6) amyloid disease. The *diagnosis* is made on the basis of the history, physical finding, examination of sputum, roentgenograms and fluoroscopy of the chest, bronchoscopy and bronchography. *Treatment* in the past has been both medical and surgical. Once the disease has established itself the former is only palliative and so the treatment of choice is lobectomy, lobectomies or pneumonectomy. The ultimate *prognosis* in untreated cases is poor, for one-third of the patients die within 1.8 years after the diagnosis is made. In the surgically treated cases it is much better and if recognized early it should be curative.

may completely empty itself and evoke a spontaneous cure. If drainage is inadequate the process will (1) spread subtly to the adjacent lung tissue to produce new abscesses, (2) spill over into adjoining bronchi and produce not only a repetition of the original trend of events but also bronchiectasis and (3) extend into the pleura to produce a putrid empyema.

The *diagnosis* is made from a careful history, roentgenograms of the chest, bronchoscopy which helps to precisely localize the lesion and bronchography which will usually demonstrate iodized oil in the surrounding bronchi but not the abscess itself. *Treatment* is at first medical by which regime it is estimated that 20 to 50 per cent of the cases will be cured. If medical treatment fails surgery is indicated, and this consists of external drainage, lobectomy and pneumonectomy. The *mortality rate* in surgically treated cases varies but in some series it has reached as high as 50 per cent.

Tuberculosis—Although tuberculosis is a systemic disease and generally in the domain of an internist, the thoracic surgeon has been able to cure a number of selected cases that otherwise would surely have been fatal. The ages of the patients operated upon have varied from fifteen to fifty-seven years, but most have been in the younger age group and three women have been treated surgically to every man. The *symptoms* are those consequent to any pulmonary tuberculosis and consist of cough, weakness, anorexia, fever, pain in the chest, loss of weight, and hemoptysis. The duration of the illness prior to operation has varied from a few weeks to eleven years. The cases chosen for pneumonectomy are those with (1) extensive multilobular predominately unilateral tuberculosis, (2) persistent bronchial ulceration or stenosis, (3) active or controlled tuberculosis associated with bronchiectasis or abscesses, (4) post thoracoplasty uncontrolled disease and (5) isolated tuberculosis. The sputum has always been positive for tubercle bacilli.

All cases that have been treated surgically have shown *gross changes* in the mucosa of the bronchi or trachea. These are always secondary to tuberculosis in the more peripheral pulmonary parenchyma, and come about by direct extension from neighboring tuberculous tissue either by way of submucosal lymphatics or perforation of extrabronchial nodes, and, less frequently, by direct implantation of tubercle bacilli from bacteria laden bronchial secretions. Heretofore knowledge regarding the bronchial and pulmonary lesions was always static and gained from an examination of autopsy material, but at the present time the bronchologist is in a unique position to observe the changes from week to week and record not only their appearance but also their progression and regression. The earliest lesions are seen in the posterior portion of the submucosa at a bronchial orifice or may extend all the way up to the trachea. The overlying mucosa is red, edematous, thickened and granular. Histologic sections at this time disclose a nonspecific reaction composed of congestion and lymphocytic infiltration, but soon small tubercles are formed between the submucosal glands. These are composed of central epithelioid cells with and without caseation and more peripherally Langhans' giant cells, plasma cells and lymphocytes.

starting point of an abscess provided the *natural defenses* of the respiratory tract are *overcome*. These defenses consist of (1) closure of the larynx which is abolished under anesthesia, (2) cough reflex which is abolished not only under anesthesia but also in sleep, (3) bacteriostatic effect of mucus and (4) action of the cilia which work in conjunction with the mucus in a given pH range. The *organisms* most frequently incriminated are Vincent's fusiform bacillus, spirochetes, *B. melaninogenicum*, vibrios and micro-aerophilic streptococci. The lesion they produce is the so-called putrid lung abscess and this, some authors maintain, is synonymous with abscess of the lung as the term is generally used.

The *lesion* is single or multiple and unilateral or bilateral. It involves the right side twice as frequently as the left and, by some authors, is said to affect the lower lobes more often than the upper



FIG. 136—Wall of a pulmonary abscess showing three zones—an inner of necrotic material, a middle of granulation tissue and an outer of fibrous tissue. $\times 37.5$.

ones. In our own material, however, the upper lobes have contained the abscess almost twice as often as did the lower lobes. The infection starts in the form of an acute focal gangrene distal to one of the smaller bronchi where the infected material is located. At first it involves only the corresponding segment of the lung but it soon spreads peripherally along the bronchioles in a wedge-shaped manner to involve the more distal lung parenchyma and the pleura. The bronchi, bronchioles and surrounding pulmonary tissue are rapidly and completely destroyed to form a foul-smelling abscess filled with pus, debris, organisms and sloughed lung (Fig. 135). The wall is first lined with detritus and granulation tissue, but the latter is soon transformed into a smooth surface (Fig. 136). The inflammatory reaction spreads to the adjacent lung parenchyma resulting in thickening and fibrosis of the septa and a complete fibrous tissue obliteration of the alveoli. Drainage of the abscess into a bronchus is usually established within two weeks. If it is adequate the cavity

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A little later the redness in the mucosa begins to wane and small ulcerations and granulations become evident. At first the basis of the ulcers are infiltrated with lymphocytes only to be rapidly replaced with tuberculous granulation tissue. This is composed of debris, caseation necrosis and epithelioid cells that make a poor attempt at tubercle formation. Initially the ulcers are small, multiple and rather shallow with the bases covered by a grey exudate. As they coalesce and enlarge they penetrate deeper until they erode even the cartilages. Some ulcers instead of enlarging



FIG 137.—Pulmonary tuberculosis There is extensive tuberculous involvement of the mucosa of the large bronchi and caseation necrosis of the periphery parenchyma. The lung was removed surgically

become smaller. The inflammation and edema subsides and, gradually, they completely heal and re-epithelialize leaving a minimum or entire absence of scarring. Those that progress, however, are associated with considerable fibrosis, and this in the end produces partial or complete cicatricial stenosis of the bronchus. The most proximal lesions are always continuous with other more distal lesions in the bronchi or bronchioles which in turn are continuous with lesions in the parenchyma. The involvement of the intermediate portions of the bronchial tree, however, may be demonstrable only histologically. In the lung itself the lesions are

usually old and as such reveal abundant fibrosis, large irregular cavernous cavities, small or large areas of caseation and irregular conglomerations of tubercles (Fig 137)

The *diagnosis* is made from the history, roentgenograms and finding the tubercle bacilli in sputum or bronchial secretions. If an endobronchial biopsy should be made by mistake it may show well-formed tubercles but more often it discloses necrotic material and nonspecific inflammation. Sometimes, however, the roentgenograms suggest carcinoma and tubercle bacilli are hard to find. In these cases we have often made a presumptive diagnosis of tuberculosis, six weeks before the culture was positive, by cytologic examination of bronchoscopically removed secretions stained by the Papanicolaou technique. Of importance in this connection are the presence of numerous islands of epithelial cells bearing cilia, giant cells of the Langhans' type and oval cells that are probably epithelioid in nature. It is to be emphasized that the *treatment* of pulmonary tuberculosis is still medical, but when the previously mentioned criteria are fulfilled surgery is indicated. The *prognosis* in this selected group of cases is relatively good.

Lipoid Pneumonia—Lipoid pneumonia ordinarily does not fall in the domain of the thoracic surgeon. Although on rare occasions it may be an indication for pneumonectomy, more commonly a lung has been removed because of a mistaken diagnosis of bronchiogenic carcinoma. The term is used to denote extensive inflammatory changes in the lungs directly brought about by a foreign oil. The *offending agents* are cod liver oil, liquid petrolatum, medicated oily preparations and milk. In infants it is often the product of forced feedings resulting from holding the nose when the child refuses to eat, and in adults it is usually brought about by spraying the nose with mineral oil or by taking it internally to relieve habitual constipation. In both infants and adults aspiration of oily material may also be accomplished in tracheoesophageal fistula, cardiospasm, laryngeal paralysis, coma and in debilitated conditions. Lipoid pneumonia occurs in infants and adults with equal frequency. Since the infantile form is not confused with carcinoma it will be omitted from further discussion. In adults the pneumonia becomes manifest in the fifth decade or later, and is found three times as frequently in men as it is in women. The lesion may be entirely *asymptomatic* or it may be *accompanied by* pain in the chest, cough, expectoration of scanty blood-tinged sputum and slight fever. It may thus simulate bronchiogenic carcinoma. Roentgenograms of the chest vary, but in the advanced stages there is often a massive shadow or a conglomeration of shadows extending from the hilum to the base of one lung. This adds further credence to a diagnosis of carcinoma.

Grossly, the early lesion resembles a lobar pneumonia in the stage of grey hepatization in that it is diffuse, grey with yellowish areas, granular, spongy and may involve the entire lobe. Later, there are present one or more firm, sharply circumscribed or ill defined nodules of varying sizes that are found near the hilum or along the bronchi of the lower lobes. The centers may contain one or more small

cavities containing droplets of oil which will characteristically float on water. *Histologically*, the alveoli at first are distorted, collapsed or emphysematous and contain vacuoles and macrophages filled with emulsified oil (Fig. 138). The septa are thickened by connective tissue, edema and lymphocytes and are lined with macrophages. Some of the latter coalesce to form giant cells. As the lesion ages there is a diffuse fibroblastic proliferation in which there remain foci of lymphocytes, plasma cells and phagocytes. The alveoli are filled with drops of oil, giant cells and foamy macrophages, and the septa are fibrotic and lined with a single layer of cuboidal cells. The draining lymph nodes disclose droplets of oil free in the

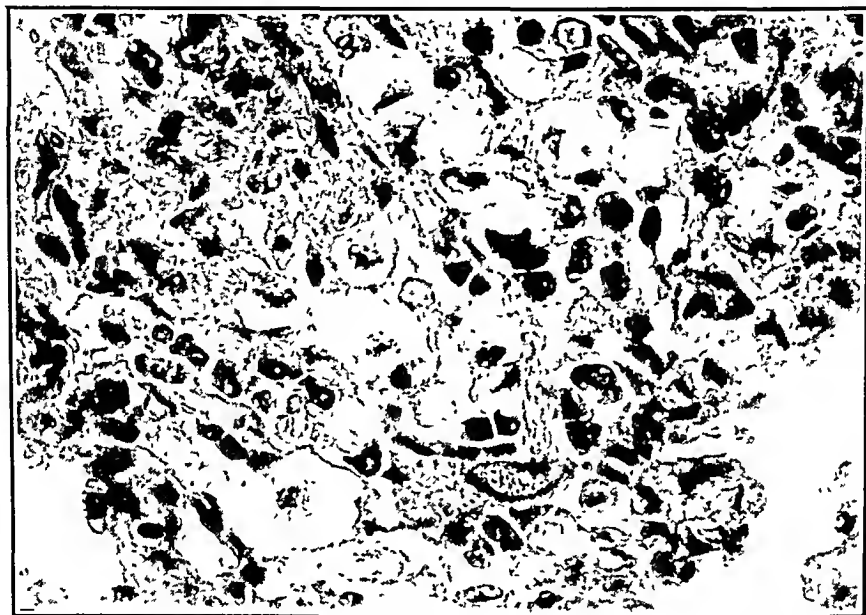


FIG. 138 —Lipoid pneumonia showing an alveolar septum tremendously thickened by an infiltration with large foam cells, monocytes, plasma cells and fibrous tissue. x 400.

sinusoids and around the follicles, foamy macrophages and patches of fibrosis.

The most important factor in making a correct *diagnosis* is eliciting a careful history. *Treatment* is usually prophylactic and symptomatic. If discovered early the *prognosis* is good, but if diagnosed late it is poor.

Tumors.—Almost all of the tissues from which the bronchus is composed have been known to give rise to benign and malignant tumors. Thus from epithelial structures there develop a papilloma, adenoma and carcinoma; from connective tissue a fibroma, myxoma, fibrosarcoma and myxosarcoma; from muscle a myoma, myosarcoma and myoblastoma; from vessels a hemangioma, lymphangioma and hemangioendothelioma; from fat a lipoma and liposarcoma; from perichondrium a hamartoma (chondroma), osteoma and osteochondrosarcoma; from lymphoid tissue Hodgkin's disease and lymphosarcoma, and from distant organs metastatic tumors. *In general* all *benign growths* are innocent only in so far as their ability to invade tissue and to metastasize is concerned, for most of them produce bronchial obstruction with concomitant suppuration and, thereby,

can cause death. Some of them are also dangerous in that, at any time, they can become malignant. Primary malignant tumors of mesodermal origin as a rule occur in relatively young patients. They start at the periphery, they merely replace the lung and produce no symptoms until they encroach upon the mediastinum or invade the chest wall. If they start more proximally they will produce bronchial obstruction and suppuration of the pulmonary segments distal to the occlusion. They remain localized for a considerable length of time and when metastasis does occur it is by way of the blood stream. Other than adenoma, hamartoma, hemangioma, carcinoma and metastatic tumors the aforementioned neoplasms are infrequent enough to be considered as curiosities and will, therefore, not be considered further.

Benign Adenoma—Benign adenoma of the bronchus has been described under many names some of which are carcinoid, cylindroma, basal cell carcinoma, benign glandular tumor, endothelioma and mixed tumor. In our own laboratory they constitute about 12 per cent of all epithelial tumors of the bronchus and to date we have examined approximately 40 cases. In contrast to bronchogenic carcinoma this tumor is found more frequently in females than in males and in about half the cases the patients are less than thirty years of age. As in other benign tumors the *symptoms* are due to bronchial irritation and obstruction, and as such consist of cough with or without expectoration, hemoptysis which may be severe enough to necessitate a transfusion of blood, wheezing respirations, fever, pain in the chest and dyspnea. In more than half of our cases the duration of symptoms, before a correct diagnosis was made, was two to eight years, thus indicating the slow growth of the neoplasm.

The tumor is found more often on the left side than on the right, is always located in the main bronchus or their immediate subdivisions, and in two-thirds of the cases it involves the lower lobe. Usually by the time the bronchologist examines the patient, the tumor partially or completely occludes the bronchial lumen. The mass is round, sessile or pedunculated, smooth or superficially ulcerated, pink, red or purple, quite firm or soft, and frequently bleeds readily when touched with the biopsy forceps. The true nature of the tumor, however, can only be ascertained when the lung is examined after pneumonectomy or at postmortem (Fig. 139). The endobronchial growth is always the smaller portion of the tumor. Its base is narrow, occupies the thickness of the bronchial wall and is attached to a round sharply demarcated extrabronchial mass that ordinarily is two or three times the size of the portion in the lumen. The entire size of the neoplasm varies, but most of the ones we have seen are 3 to 6 cm. in diameter. On cut surface the tumor is gray pink or hemorrhagic sometimes with small areas of frank necrosis and occasionally exhibiting bone or cartilage. By the time the pathologist receives the specimen, the bronchi distal to the tumor are greatly dilated and filled with pus and the surrounding lung tissue is atelectatic and fibrotic.

The *histologic* picture varies a great deal from tumor to tumor but is quite constant throughout the same tumor even when successive

biopsies are removed years apart (Figs. 140 and 141). The surface is always covered with bronchial epithelium which may be attenuated, superficially ulcerated or metaplastic. The basement membrane ordinarily is distinct and intact although rarely it is broken and cords of basal from the epithelium descend into the submucosa where they are continuous with the tumor proper. Beneath the basement membrane there is usually a thin or broad band of dense or edematous and vascular connective tissue which separates the neoplasm from the mucosa. The tumor is composed of two basic elements—epithelial cells and supporting stroma. Although the former vary from tumor to tumor they have one characteristic in



FIG. 139 —Benign adenoma The endobronchial portion only is seen. It is large, round, smooth and pedunculated. The bronchi distally are greatly dilated.

common. They are always regular. They are arranged in whorls, nuggets, sheets, cords or glands. The latter are really not true glands but appear rather as clusters of cells in some instances surrounding capillaries and, in others, empty spaces which apparently are derived from a myxomatous degeneration of the epithelial cells themselves. The pseudoglands frequently contain strands of bluish stained mucoid material and partly degenerated epithelial cells. The tumor cells are slightly larger than the basal cells of the mucosa. They are polygonal or oval and usually have an abundant amount of ill-defined pink or slightly basophilic cytoplasm. In most tumors the nuclei are round or oval, evenly stained and vesicular, but, at times, they are more spindle and quite pycnotic. Usually they are centrally placed and single although, occasionally, they are eccentric,

double and when the cells are disunited they bear some resemblance to plasma cells. The stroma likewise varies in quantity and quality. In some tumors it is scanty and almost imperceptible whereas in others it forms thin or broad strands of connective tissue that separate masses of epithelial cells. It may be loose, dense, collagenous, edematous or frankly myxomatous and may contain a few or many engorged capillaries and sometimes large lakes of extravasated erythrocytes. Inflammatory cells in the stroma are inconspicuous but when present consist of a few plasma cells and lymphocytes. The above are the only elements encountered in an examination of endoscopically removed tissue. When one examines an entire

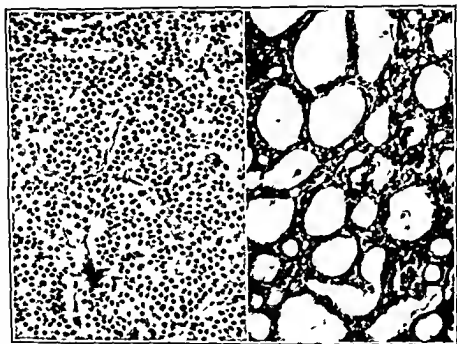


FIG 140

FIG 141

FIG 140—Benign adenoma showing sheets of very uniformly staining cells with abundant ill defined cytoplasm. The stroma is scanty but very vascular. $\times 200$

FIG 141—Benign adenoma showing pseudoglands that contain strands of bluish stained material and degenerating epithelial cells. $\times 200$

specimen, however, one occasionally finds near the pedicle connecting the two masses of tumor bits of cartilage and bone. The former is, practically always, much in advance while the latter is quite conspicuous. Both are regular but the bone often exhibits an intense hyperplasia of the marrow cells. Ordinarily the tumor remains localized for many years though at any time it may become cancerous and extend not only to other portions of the same lung but also metastasize to the draining lymph nodes and distant organs.

Although all authors agree that the tumor is epithelial in nature its histogenesis is still in dispute. It has been considered to arise from the basal cells of the bronchial epithelium, from submucosal glands, from oncoocytes and from misplaced embryonal bronchial

buds which in later life undergo neoplasia and form a true mixed tumor. The latter concept has been based on finding pieces of cartilage, bone and, allegedly, muscle in the tumor. We have not been able to identify muscle but we have found cartilage and bone in some of our cases. Of these only the bone is hyperplastic whereas there is no more cartilage than is usually found in a normal bronchial wall. In no instance, however, have either been an integral part of the tumor. Rather they are usually found in a focal area of not more than 1 cm. in diameter and in the narrow or mural portion of the tumor. The cartilage is a residuum of the bronchial wall and the bone develops from the perichondrium as a result of long-continued irritation by the tumor. Similar proliferations of osseous tissue are frequently seen in other irritative lesions, as for example bronchiectasis. Because of the varied histologic structure of the tumor with, at times, a resemblance to (1) cystic basal cell carcinoma of the skin, (2) adenoma of the parotid or submaxillary glands and (3) oncocytes which among other places are found in the salivary glands and submucosal glands of the trachea and bronchi, it is my opinion that benign adenoma is not a single tumor but a group of tumors that arise from basal cells of the mucosa, from submucosal glands and from oncocytes.

The *diagnosis* is made (1) from ordinary roentgenograms of the chest which show atelectasis or bronchiectasis with or without a circumscribed tumor, (2) from tomograms which precisely outline the tumor and (3) from a bronchoscopic examination at which time the tumor is visualized and a portion removed for histologic study. Formerly, *treatment* was endoscopic removal or electrocoagulation of the tumor, but because of the collar-button-like nature of the growth and its potentially cancerous tendency the consensus at the present time is lobectomy or pneumonectomy. If such treatment is carried out the prognosis is excellent. If treated locally or not at all, *death* results from bronchiectasis, pneumonia, malignant transformation of the tumor or unrelated causes.

Hamartoma.—Hamartoma of the lung, as in any other organ, implies a tumor composed of normal tissues abnormally arranged. In reality it is actually a chondroma which has epithelial and mesodermal elements added. Many of the tumors have been discovered as an incidental finding at necropsy but since some are picked up during life they are of clinical importance. Most of them are entirely *asymptomatic* although dyspnea on exertion, burning sensation in the chest and cough have been described. They occur with equal frequency in both sexes and have been encountered most often after the age of fifty years.

The *tumor* involves one lung as often as the other, is usually situated subpleurally and varies in size from a few millimeters to one that fills the entire hemithorax. It is sharply circumscribed, lobulated, hard and on section the only grossly recognizable tissue is cartilage containing areas of calcification and ossification. Sometimes there are cysts between the islands of cartilage and, rarely, a bronchus may be seen entering a tumor mass. *Histologically*, islands of adult or embryonic cartilage are surrounded by bands of

connective tissue which has a tendency to undergo mucoid degeneration (Fig 142). Foci of adult bone with well-developed marrow are quite frequent. At the periphery, both the cartilage and the bone are covered with columnar or cuboidal epithelium which may or may not be ciliated and which often secretes mucus in variable quantities. Fatty tissue is found quite regularly and smooth muscle rarely. The tumor is benign, but a change to an osteochondrosarcoma has been reported.

If the diagnosis is made during life it is based on roentgenograms which show a mass of greater intensity surrounded by normal lung and exhibiting sharp lobulated borders and inner areas of calcification or ossification. Treatment is enucleation, lobectomy or pneumectomy depending upon the size of the tumor. The prognosis is excellent.



FIG 142—Hamartoma. There are several islands of cartilage surrounded by connective tissue which is covered with regular epithelium. $\times 50$.

monectomy depending upon the size of the tumor. The prognosis is excellent.

Hemangioma—Hemangioma of the lung has also been described under *pulmonary arterio venous fistula*. It is uncommon and is one of the few intrathoracic tumors that can be diagnosed correctly without resort to a biopsy. The tumor is really a mass of blood vessels connected with both the pulmonary arteries and veins, thus producing a shunt between the two circulations. As a result some of the blood passes through the lungs without being oxygenated. Consequently, the patients characteristically develop dyspnea, clubbing of the digits, cyanosis and polycythemia. Roentgenograms of the chest disclose non-specific pulmonary shadows of increased density in one or both lung fields. Pathologically, the tumors vary in size from 3 to 8 cm, are located in any portion of the lung, are solitary or multiple, and are composed of a spongy mass of dilated vascular channels or well developed cystic spaces filled with blood. If dissected carefully both arterial and venous connections with the tumor can usually be demonstrated. Microscopically the neoplasms

are composed of endothelial lined cavernous spaces containing erythrocytes. They do not produce metastases. The chief *complication* is massive hemorrhage which may be fatal. As a result of polycythemia there may be exhaustion of the bone marrow, granulocytopenia or thrombosis. The *prognosis* is thus grave. The *treatment* of choice is local excision, lobectomy or pneumonectomy.

Carcinoma.—Primary carcinoma of the lung is a common disease. In the United States it is responsible for about 6000 deaths a year. Due to refinements in modern methods of diagnosis there is little doubt that the disease is being recognized more frequently now than it has been in the past. Most chest specialists are of the opinion that there has been not only an apparent but also an actual increase in its frequency, but those who have taken the trouble to compile statistics are of the opinion that there has been no real increment. Nevertheless, at the present time it constitutes about 10 per cent of all cancers and is considered as the fifth most common carcinoma in males. It occurs at any age from infancy to the eighth decade but is usually seen beyond the age of forty years and at an average of about fifty years. From 75 to 90 per cent of the cases are found in males and the white race is affected one and one half times as often as the colored. There are no early *symptoms* in carcinoma of the lung and for this reason the physician must be forever mindful of the possibility of this disease in every patient presenting complaints referable to the chest. At the present time, 60 per cent of pulmonary carcinomas are incorrectly diagnosed and treated for twelve months or more. What a waste of precious time! The presenting symptoms in order of frequency are cough which initially is irritating and dry but later productive, pains in the chest, dyspnea, hemoptysis, loss of strength, loss of weight, anorexia, fever, night sweats, wheezing respirations and hoarseness.

The *cause* of carcinoma is a conundrum. Almost every disease that affects the lungs and every material inhaled with the air has been considered of etiologic importance on the premise that chronic irritation is a predisposing factor. Among these have been (1) inflammation such as pneumonia, influenza, asthma, tuberculosis, bronchiectasis, chronic bronchitis and abscess, (2) pneumoconiosis particularly silicosis and asbestosis and (3) inhaled substances as gas, tobacco smoke, automobile fumes and sublimates of tar. Despite their incrimination, however, none of these has been definitely proved to be a causative factor.

Except for an occasional origin from the submucosal glands or ducts, primary carcinoma of the lung probably always *arises* from the basal cells of the mucosa. This question has already been discussed in the section on carcinoma of the trachea (p. 162). It must be added, however, that many authors believe that a primary carcinoma can arise in the epithelial cells lining the alveoli and have referred to this as alveolar cell carcinoma. Such a premise presupposes that the alveolar septums are lined with or contain epithelial cells—a question which has aroused much controversy and is far from settled. These cells are somewhat nebulous to say the least, for they are never recognizable in routine sections of normal lungs.

The problem is too complicated and perhaps too academic to discuss at length here. It is sufficient to say that carcinoma probably does not arise in the alveoli and that tumors so designated are primary bronchogenic and metastatic adenocarcinoma whose original sites were not found.

Carcinoma of the lung involves each lung with approximately equal frequency, and is said to be located in the main bronchi or their first subdivisions in about 75 per cent of the cases and at the periphery in only 3 per cent. These figures are probably incorrect. Our own experience has been that only 42 per cent are located near the hilum and most of the rest are at the periphery. Seldom does one have the opportunity to examine an early carcinoma unless it is an incidental finding or unless hemoptysis is an alarming initial

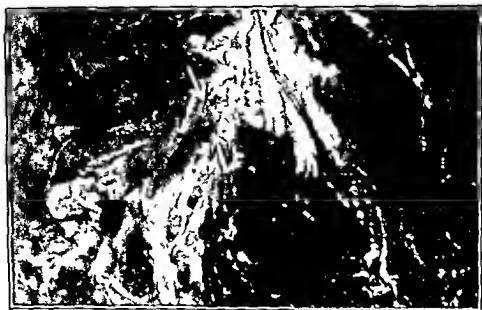


FIG. 143.—Very early carcinoma of a main bronchus showing only granularity of the mucosa.

symptom. In such cases the *first change* in the mucosa is a loss of the normal luster to be followed by an irregular, fine granularity of the surface (Fig. 143). The area may be small or initially involve 2 to 4 cm. of the epithelium. At first the lesion is confined entirely to the mucosa, but soon it penetrates to the submucosa, the cartilages and beyond where it may measure many centimeters in diameter. Concomitantly it spreads around the lumen and, as it does so, it narrows and then completely constricts the bronchial orifice (Fig. 158). This type of tumor is usually greyish-white, extremely firm and when large contains irregular areas of necrosis and hemorrhage. *Less frequently* the tumor starts in a small area of the mucosa and projects into the lumen as a large polypoid mass that may be confused grossly with a benign adenoma (Fig. 144). In contrast, however, the cancer is firmer, more greyish white, less vascular and its attachment to the wall is, as a rule, somewhat

broader. As in the stenosing type of carcinoma, so as in the polypoid, the wall is destroyed and the extension of the tumor beyond the bronchus reaches similar proportions. In either case the growths produce bronchial obstruction that is always accompanied by varying degrees of bronchiectasis and abscess formation in the distal segment of the lung. In the more *peripherally* located tumors the point of origin is often difficult or impossible to find. These tumors are grossly similar to pulmonary extensions from the more proximal growths and as such take on one of three appearances; (1) they are composed of large or small, sharply circumscribed, centrally necrotic masses of grey, firm tumor tissue pushing the lung parenchyma aside and destroying that which it infiltrates (Fig. 145),

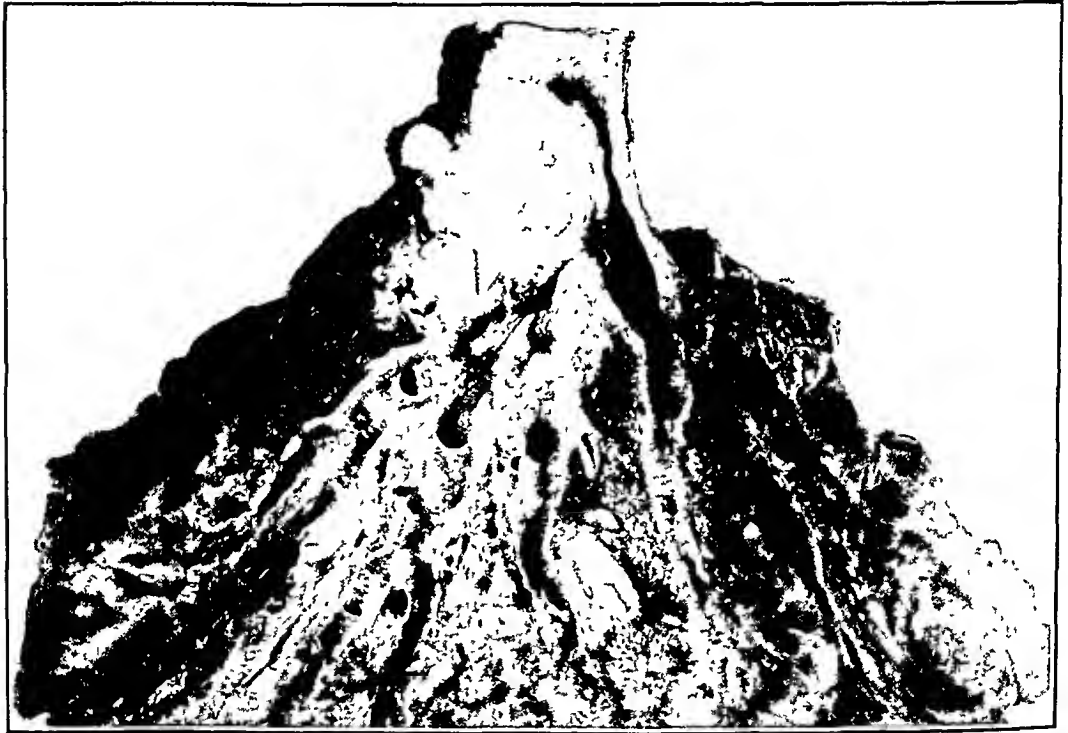


FIG. 144.—Polypoid carcinoma of a main bronchus The tumor has straddled the wall and almost completely occluded the bronchial lumen

(2) they resemble focal or lobar pneumonia in the stage of grey hepatization, that is, they are firm but ill defined, infiltrate to but do not destroy the pleura and do not entirely obliterate the underlying pulmonic architecture and (3) they superficially look like miliary or conglomerate tuberculous pneumonia. On closer inspection, however, the nodules in carcinoma vary a great deal more in size than do tubercles and the larger ones do not show the caseation that conglomerate tubercles of this magnitude usually do.

Histologically, carcinoma of the lung is one of the most pleomorphic of all carcinomas. For this reason it is difficult to classify precisely, and the best that one can do is to state which type of tissue predominates. The cellular variation is evident not only in the metastasis as compared with the primary growth but even in a single microscopic field. Nevertheless, three broad groups are

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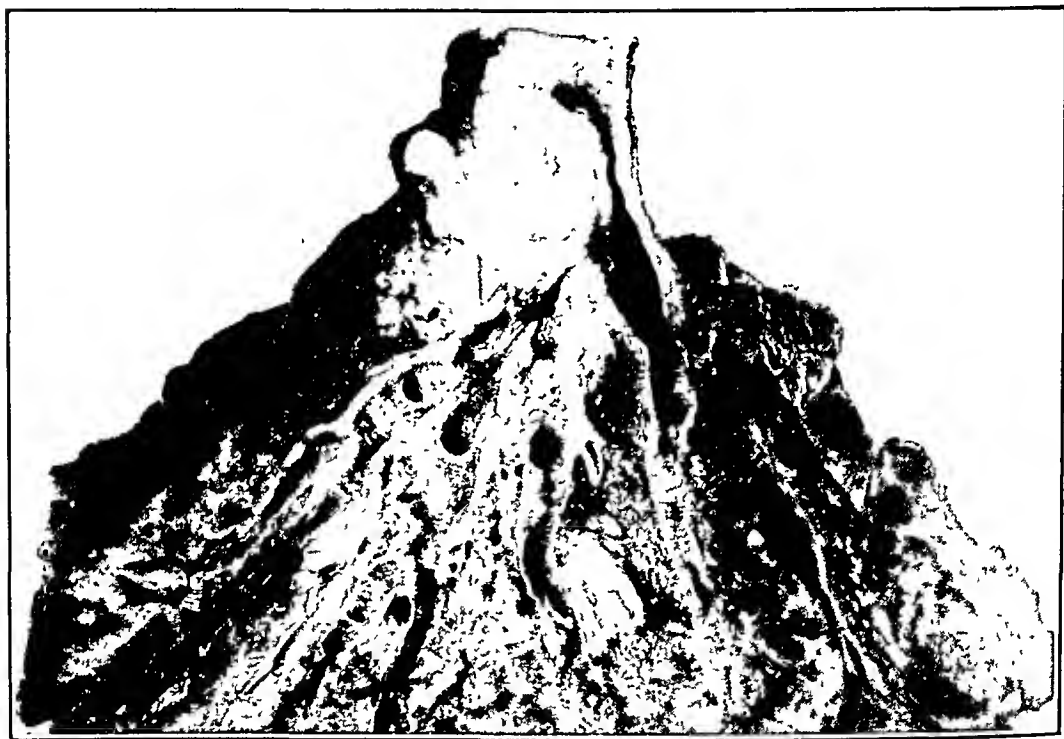


FIG. 144.—Polypoid carcinoma of a main bronchus. The tumor has straddled the wall and almost completely occluded the bronchial lumen.

(2) they resemble focal or lobar pneumonia in the stage of grey hepatization, that is, they are firm but ill defined, infiltrate to but do not destroy the pleura and do not entirely obliterate the underlying pulmonic architecture and (3) they superficially look like miliary or conglomerate tuberculous pneumonia. On closer inspection, however, the nodules in carcinoma vary a great deal more in size than do tubercles and the larger ones do not show the caseation that conglomerate tubercles of this magnitude usually do.

Histologically, carcinoma of the lung is one of the most pleomorphic of all carcinomas. For this reason it is difficult to classify precisely, and the best that one can do is to state which type of tissue predominates. The cellular variation is evident not only in the metastasis as compared with the primary growth but even in a single microscopic field. Nevertheless, three broad groups are

the alveolar spaces similar to a pneumonic exudate and leave the septa intact.

Adenocarcinoma is considerably less frequent than the squamous cell variety. In the bronchial wall, the peribronchial tissue and metastatic lesions, the cells are arranged in irregular acini supported by varying amounts of a vascular, loose or dense fibrous tissue stroma. In the lung parenchyma, however, they use the septa as a scaffolding and are characteristically disposed about the periphery of the alveoli (Fig. 147). Frequently, they form papillary or more

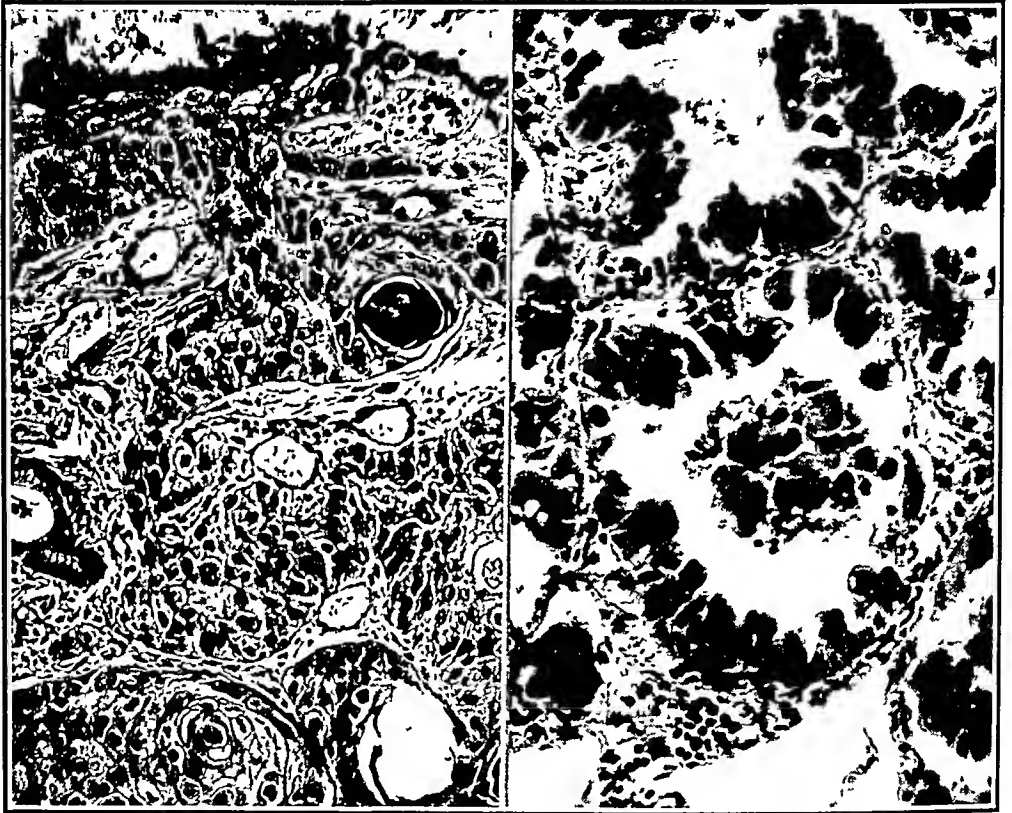


FIG. 146

FIG. 147.

FIG. 146—Squamous cell carcinoma of the lung The submucosa is infiltrated with irregular strands of epithelial cells containing one pearl. x 100

FIG. 147.—Adenocarcinoma of the lung showing alveoli lined with several layers of tall cuboidal cells x 200.

solid masses that project into the lumen and resemble renal glomeruli. The cells are low cuboidal, tall cuboidal or columnar. Sometimes they form a single peripheral layer, but at other times they are 2 to 4 cells deep. The cytoplasm is homogeneously deep pink or contains vacuoles filled with mucoid material. At times, this is so abundant that it streams forth in long strands to fill the lumen of the acini. The nuclei as a rule are quite regular, round or oval and deeply but regularly stained. There may be several in a single cell. Mitoses are not abundant.

Fortunately, a tumor predominantly of the *anaplastic* cell type is the least frequent for it is also the most rapidly growing. Its cells are even more irregular than are those of the other two groups. They are (1) oval or spindle shaped and commonly called "oat cell"

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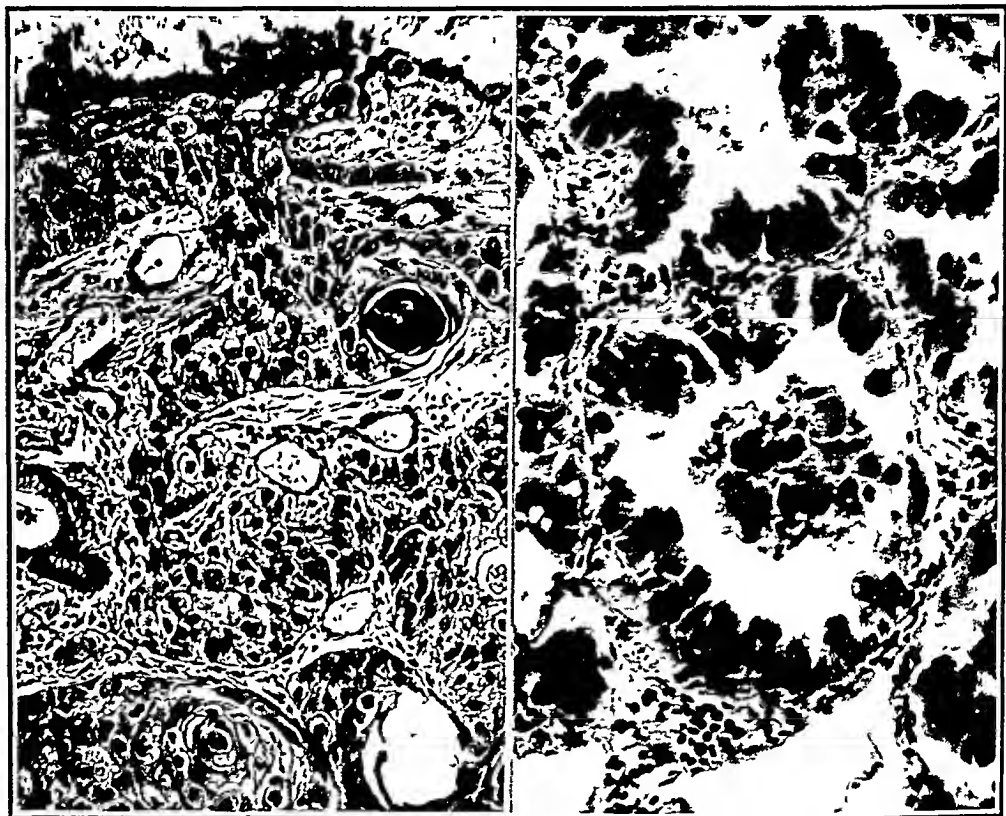


FIG. 146.

FIG. 147.

FIG 146.—Squamous cell carcinoma of the lung. The submucosa is infiltrated with irregular strands of epithelial cells containing one pearl x 100.

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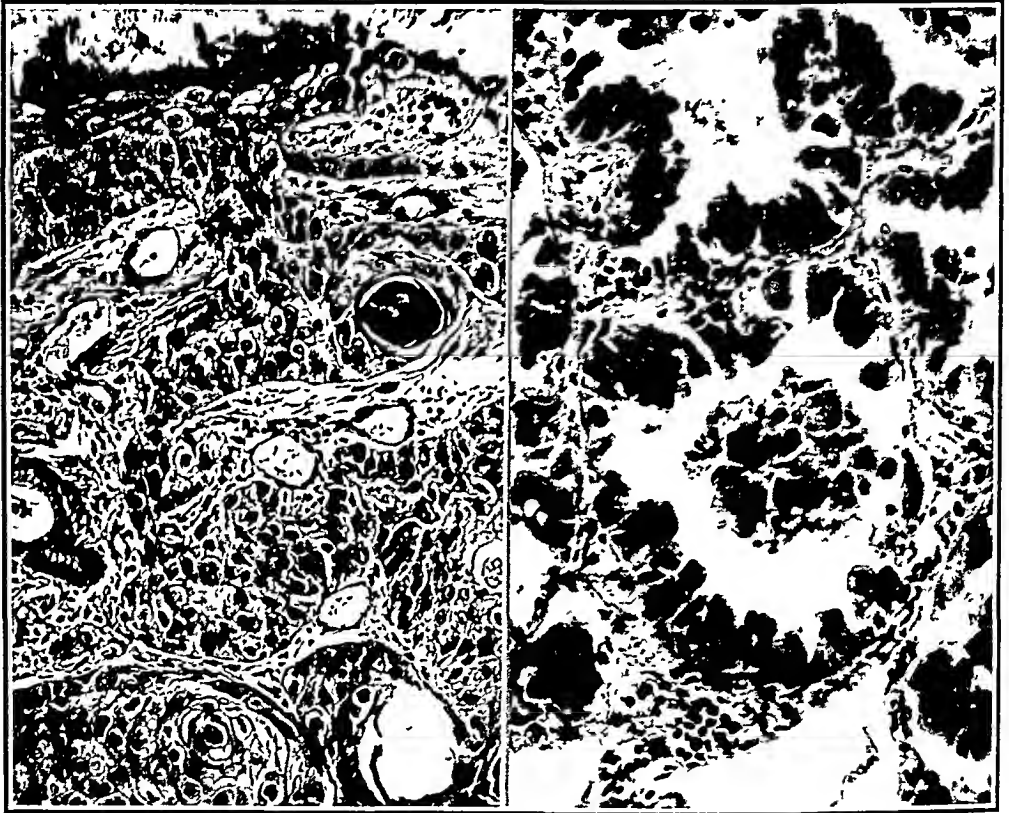


FIG. 146

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lungs are examined at necropsy. As already inferred the tumor *extends* to the surrounding lung tissue, pleura and mediastinum. When it reaches the pleura it usually produces a hemorrhagic or serous effusion the sediment of which often contains cancer cells. In the mediastinum it infiltrates the lymph nodes, blood vessels, pericardium, heart, trachea, esophagus and recurrent laryngeal nerve. The latter results in laryngeal paralysis. Encroachment upon the veins produces edema of the upper extremities, head and neck if the superior vena cava is involved, and ascites with edema of the lower extremities if the inferior vena cava is occluded. Direct extension to the thoracic inlet produces the *Pancoast syndrome* which is discussed in the section on the pleura. Distant *metastases* in approximately the order of frequency occur in lymph nodes, liver, adrenals, kidneys, opposite lung, bones, brain, spleen and pancreas.



FIG 150 —Secretions removed at bronchoscopy from the same case illustrated in figure 145. There are numerous single cancer cells and one well-formed pearl Papanicolaou stain. x 400.

Cancer of the lung is so incipient that often by the time there are any symptoms, it is already too late. To wait for a characteristic history is to court with disaster. *Roentgenograms* of the chest are of the greatest value in picking up shadows which can then be further investigated by *fluoroscopic examination*, *tomograms* and *bronchograms*. *Bronchoscopic examination* is of inestimable importance in making a positive diagnosis by visualizing the tumor and securing both tissue for histologic study and secretions for cytologic examination. Reports in the literature indicate that tissue can be secured in 75 per cent of the cases. Our own experience has been that it can be obtained in only 42 per cent of the cases for the remaining growths are peripheral and beyond the reach of the bronchoscope. In an additional 40 per cent, however, we have been able to make a positive *cytologic diagnosis* of carcinoma by finding cancer cells in *bronchial secretions* (Fig. 150). A morphologic diagnosis is also made by aspiration of the tumor through the chest

will (in selected cases), at exploratory thoracotomy, and when the disease has advanced beyond the curable stage from cells in the pleural effusion, metastatic nodules and, of course, at necropsy. The only effective *treatment* is pneumonectomy with removal of the draining lymph nodes. The *prognosis* is grave for the five year survival rate in the best clinics is only 5 to 8 per cent. Untreated patients are usually dead within a year.

Secondary tumors of the lungs are very common. In hospitals where there is an active department of bronchology, the ratio of primary to secondary pulmonary neoplasms in cases coming to necropsy is about equal, but in an ordinary hospital the latter exceeds the former. Because the lungs receive venous blood from all parts of the body, it is only natural that tumors metastasizing by way of the blood stream should lodge in the small pulmonary capillaries. Our own material consists of 125 cases of carcinoma and about 30 cases of sarcoma with metastases to the lungs encountered in a total of 600 necropsies on patients with neoplasms. The *primary sites* are in the skin, sinuses, breast, mucous membranes of the mouth, thyroid gland, gastrointestinal tract, liver, gall bladder, pancreas, adrenal glands, genito-urinary system, bones and bone marrow.

Surprisingly enough, both the *gross* and *microscopic* distribution closely simulates primary neoplasms of the lung. There is only one exception. Rarely do secondary pulmonary tumors invade the mucosa of a larger bronchus to produce obstruction of the lumen with atelectasis and bronchiectasis distal to the occlusion. This, as already stated, is common in primary bronchogenic growths. Metastatic tumors to the lungs, however, are usually indistinguishable both grossly and roentgenologically from primary peripheral tumors of the lung. In each there are a few or many, sharply circumscribed or ill-defined, single or confluent nodules measuring from less than a millimeter to many centimeters in diameter, or there is a diffuse pulmonic infiltration that is difficult to distinguish from ordinary pneumonia. The *microscopic* distribution of metastatic pulmonary tumors is likewise similar to that of primary neoplasms in the lungs. The perivascular and peribronchial lymphatics, the blood vessels and the bronchi all contain tumor cells. In the lung parenchyma neoplastic cells are distributed in three definite patterns with transitions from one to the other. First, in tumors accompanied by fibrous tissue the arrangement is in irregular nests or masses of cells that completely destroy the underlying pulmonary parenchyma. Second, when the cells are anaplastic or in solid formation and unaccompanied by fibrous tissue, they are frequently deposited within the alveolar lumens in a manner similar to a pneumonic exudate. Third, when the tumor is a pure adenocarcinoma the cancer cells line the alveolar septa.

The *diagnosis* of metastatic pulmonary neoplasms is made by finding the primary site in some other organ. Ordinarily, the *prognosis* is hopeless and *treatment* is palliative. There is only one exception to this rule. A solitary pulmonic metastasis, occurring several years after a primary tumor in some other portion of the body has been eradicated, may be cured by lobectomy or pneumonectomy.

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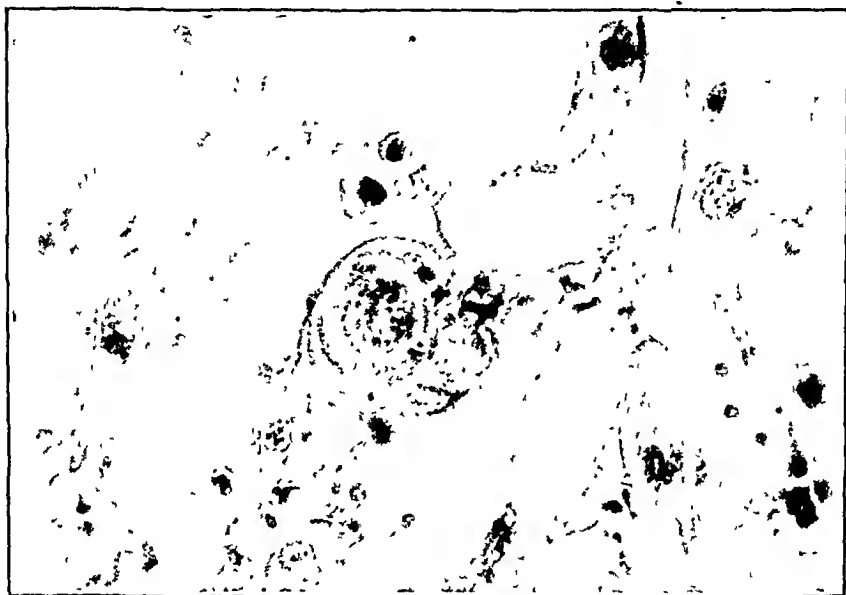


FIG 150—Secretions removed at bronchoscopy from the same case illustrated in figure 145. There are numerous single cancer cells and one well-formed pearl. Papanicolaou stain x 400

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all the lobes. This includes bronchiectasis, cystic disease, abscess and, rarely, chronic fibrous pneumonitis, lipoid pneumonia and fungus disease. (3) Selected cases of pulmonary tuberculosis.

Postoperative Pulmonary Complications—There are two post-operative pulmonary complications that merit mentioning (1) atelectasis and pneumonia, and (2) embolism. Atelectasis followed by pneumonia is perhaps the more frequent. Atelectasis is a collapse of a lung or a portion of a lung. It is found most often after upper abdominal operations and, particularly, after those on the gastro-intestinal tract. Patients with chronic cough and expectoration are especially addicted, and since this occurs more frequently in men so does the atelectasis. The causes of postoperative atelectasis are (1) bronchial secretions which obstruct the lumen, and accumulate as a result of pre-existing inflammation, aspiration from the upper respiratory tract during anesthesia and, sometimes, as a result of the irritating action of the anesthetic, (2) abolition of cough reflex during anesthesia and (3) limitation of respiratory exertions. This may be due to pain, tight binder, and in males, who are diaphragmatic breathers, splinting of the diaphragm particularly after upper abdominal operations. Pathologically, the degree of collapse varies from involvement of a portion of one lobe to massive involvement of both lungs. The affected areas are decreased in size, deep red to purple and non-crepitant. Cut surfaces show mucus in the bronchi and edema fluid in the parenchyma which in time is replaced by pneumonia.

Pulmonary emboli following operations are probably quite common, but only a few produce symptoms. The incidence of clinically apparent emboli is about 0.23 per cent. They usually occur from six to ten days after operation and are manifest by sudden pain in the chest, hemoptysis, dyspnea, pleural friction rub, moderate leukocytosis and fever. Patients over fifty years of age are affected most frequently, and fatalities are highest in those over sixty years. Males are victims more often than females in the ratio of 3 to 2.

The source of the embolus may be the operative site, but in 27 per cent of the cases it arises from symptomless thrombi in the legs and in many other cases from the pelvic and iliac veins. The size of the pulmonary vessel that is occluded, depends entirely upon the size of the embolus, and each dictates the size of the infarct. The lower lobes are involved in 74 per cent of the cases and the right side is affected a little oftener than the left. Infarcts are always located at the periphery of the lung and usually where two or more pleural surfaces converge. At first, they are ill-defined, deep red and are indistinguishable from hemorrhagic pneumonia or simple hemorrhage. Gradually, the borders become sharper giving them a definite shape (Fig 151). They are rarely, if ever, actually triangular although they may be roughly pyramidal. The long axis is always parallel to the longest pleural surface involved and the cardiac margin is rounded or humped. In the second week, the color changes from bright red to dark red or almost black, and they begin to decrease in size. This continues for weeks or months until they are completely healed and are replaced by a depressed scar.

If the interval between the two, however, is short such a procedure is not justified.

Mechanical Disturbances.—Under this heading will be included (1) bronchial fistulas, (2) indications for pneumonectomy, (3) post-operative pulmonary complications, (4) foreign bodies, and (5) trauma. The causes of bronchial obstruction have already been tabulated in the section on bronchiectasis (p. 170).

Bronchial Fistulas.—A bronchial fistula is a communication between a bronchus and another hollow organ or a cavity. There are only two that are common, namely, bronchopleural and bronchoesophageal. They are distressing because the former becomes associated with a chronic empyema, which will persist until the bronchus is closed, and the latter produces fatal pulmonic supuration unless the ostium is obliterated. The *causes* of bronchial fistulas are three—inflammation, cancer and trauma. *Inflammation* may be acute but is usually chronic and accompanies empyema, pulmonary abscess and bronchiectasis. Of particular importance is tuberculous infection. In bronchopleural fistula it usually follows a tuberculous empyema or a rupture of a caseous pulmonic nodule or tuberculous cavity, and in a bronchoesophageal fistula it is due to a breakdown of a caseating tuberculous lymph node. *Cancer* is a common cause of bronchoesophageal fistula but does not directly produce a fistula between a bronchus and the pleural cavity. The former is almost always the result of a primary carcinoma of the esophagus because this cancer has a tendency to deep ulceration. The cancerous lesion may be insignificant whereas the consequent pneumonitis, bronchiectasis and abscess may produce overwhelming symptoms and be the cause of death. *Trauma* is an important etiological agent of both bronchio-pleural and bronchoesophageal fistulas. The former most frequently results from operative procedures such as lobectomy, pneumonectomy and even thoracotomy, when an injudiciously placed hard rubber tube may produce ulceration of the lung and a communication of the more peripheral portion of the bronchial tree with the pleural cavity. Traumatic bronchoesophageal fistula is most often caused by swallowed, irregularly pointed, foreign bodies. The opening is usually into the trachea or left main bronchus.

Indications for Pneumonectomy.—Pneumonectomy is a recent operative procedure dating back to April 1933. It may be defined as a complete surgical removal of one lung in a single stage, and is accomplished by separate ligation of each of the hilar structures and by closure of the severed bronchial stump. The indications for pneumonectomy are rather rigidly followed and consist of: (1) *Primary pulmonary neoplasm.* The chief one of these, of course, is bronchogenic carcinoma provided the tumor has not progressed far enough to be accompanied by bloody pleural fluid, paralysis of the diaphragm, paralysis of the left vocal cord, pain in the thoracic wall or down the arm, extension into the trachea and distant metastases. Other tumors that are indications for pneumonectomy are bronchial adenoma, sarcoma and large benign neoplasms. (2) *Chronic non-specific suppuration* that is unilateral and involves

tremely variable. They can be classed as (1) vegetables consisting of peanuts, corn, beans, watermelon seeds and timothy heads, (2) bones due to carelessness in preparing and eating food (found more commonly in adults with dentures) and (3) manufactured objects such as coins, discs, buttons, dental plates, false teeth, safety pins, tacks, screws, beads, ammunition, jewelry and tags (Fig 153). The duration of lodgement varies from a few minutes to many years. The most common immediate *symptom* is dyspnea due to an obstruction resulting from a concomitant septic laryngotracheobronchitis. This is brought about most often in cases of vegetable foreign bodies and is usually seen in infants and young children. Later *complications* consist of bronchiectasis, empyema, and pulmonary abscess.

The *diagnosis* is made from the history, roentgenogram which will reveal metallic bodies or the sequelae of non-opaque objects, and visualizing the foreign body bronchoscopically. *Treatment* is re-

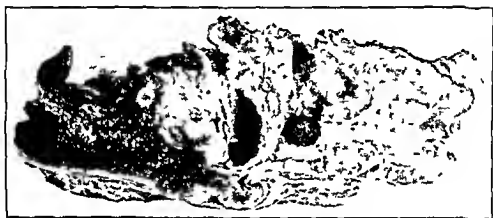


FIG 153—Bullet in a bronchus aspirated fifty four years previously. There is extensive bronchiectasis and complete fibrosis of the lobe.

moval of the object with the aid of the bronchoscope and appropriate attention to the complications as they arise. The *prognosis* is good. The *mortality* is in the neighborhood of 3 per cent.

The most common *endogenous* foreign bodies, excluding inspissated secretions or caseating tissue, are *broncholiths*. The *synonyms* are *pulmoliths*, *bronchial stones*, *calculi* and *lung stones*. They may form within the lumen of the bronchus or in the pulmonary parenchyma and migrate into the bronchus. The most common *cause* is calcification of tuberculous material and less often of pus from an abscess, empyema or bronchiectatic cavity. They vary from a few millimeters to several centimeters in length and are usually multiple, hard or soft, irregular and greyish white. *Symptoms* usually accompany their migration and consist of cough, substernal pain, hemoptysis and recurring attacks of infection. The *ages* of the patients vary from twenty to seventy years. As in aspirated foreign bodies, the *complications* are bronchiectasis, empyema and abscess. The *diagnosis* is made when one or more calculi are expectorated or when they are viewed with the aid of a bronchoscope.

Histologically, in the first two days, there is congestion of the capillaries and diapedesis of erythrocytes into the alveoli. Necrosis of the alveolar walls and erythrocytic disintegration begins after the second day and granulation tissue appears at the periphery in the second week (Fig. 152). The latter ultimately transforms the infarct into a fibrous tissue scar. Granulation tissue from the inner wall of the vessel likewise penetrates the thrombus in the pulmonary artery and converts it into a fibrous tissue core. Later it becomes recanalized. The *complications* of pulmonary infarct are pleural effusion, pulmonopleural fistulas, empyema and abscess.

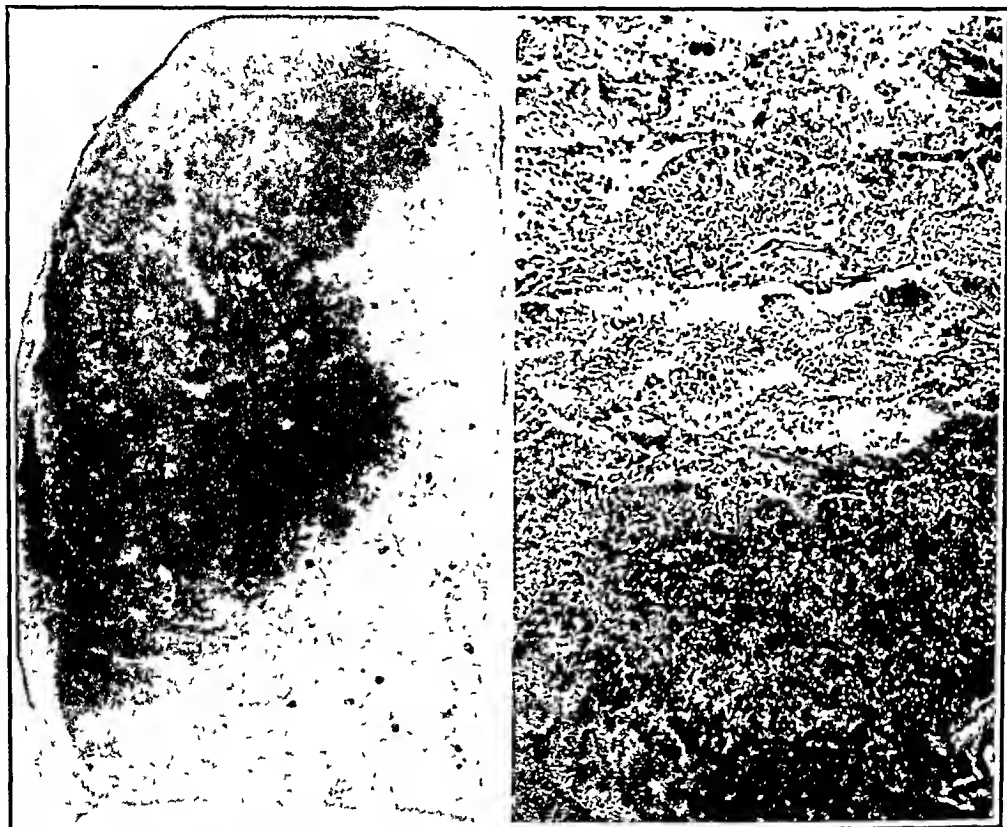


FIG. 151.

FIG 152.

FIG 151 —Pulmonary infarct.

FIG 152 —Infarct. Erythrocytic extravasation has destroyed the lung parenchyma in the infarcted area. The adjacent lung tissue is well-preserved x 75.

The *diagnosis* is made from the history, roentgenograms of the chest and, of course, at autopsy. The *treatment* is early ambulation, anticoagulation therapy and prophylactic femoral vein ligation. The *prognosis* in symptomatic emboli is guarded, for 20 per cent of the patients die. Of these 50 per cent die within ten minutes, 75 per cent within half an hour and 90 per cent within an hour.

Foreign Bodies.—Foreign bodies in the bronchi can be divided into *exogenous* and *endogenous*. The former are much more common and consist of objects aspirated into the tracheobronchial tree. As already stated, once an object passes the laryngeal barrier it also passes through the trachea and lodges in the bronchi. Most of the patients are infants or children and the objects aspirated are ex-

tremely variable. They can be classed as (1) vegetables consisting of peanuts, corn, beans, watermelon seeds and timothy heads, (2) bones due to carelessness in preparing and eating food (found more commonly in adults with dentures) and (3) manufactured objects such as coins, discs, buttons, dental plates, false teeth, safety pins, tacks, screws, beads, ammunition, jewelry and tags (Fig 153). The duration of lodgement varies from a few minutes to many years. The most common immediate *symptom* is dyspnea due to an obstruction resulting from a concomitant septic laryngotracheobronchitis. This is brought about most often in cases of vegetable foreign bodies and is usually seen in infants and young children. Later complications consist of bronchiectasis, empyema, and pulmonary abscess.

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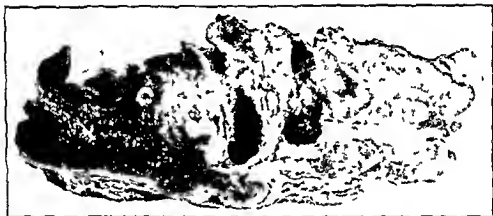


FIG 153—Bullet in a bronchus aspirated fifty-four years previously. There is extensive bronchiectasis and complete fibrosis of the lobe.

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Some patients cure themselves by coughing up the broncholiths but, frequently, this method must be supplemented by bronchoscopic removal. The complications are treated separately.

Trauma.—Trauma to the lungs or bronchi is usually associated with trauma to the thoracic cage and pleura and this will be considered in the ensuing section. *Rupture* of a main bronchus from indirect external injury, however, has been reported several times. There is usually a history of previous trauma, particularly an automobile accident, which dates back a few months or many years. The condition may now be accompanied by dyspnea on exertion or it may be entirely asymptomatic. A roentgenogram shows a diffuse density of the lung with a pulling of the trachea and mediastinal structures to the affected side. A bronchoscopic examination discloses a complete fibrous tissue occlusion of the main bronchus. The *mechanism* of rupture resulting from non-penetrating injury is allegedly due to a compression of the bronchus between an elastic anterior and rigid posterior wall. This is possible only in the presence of increased intrabronchial pressure caused by a closed glottis when the lungs are in an inspiratory phase.

PLEURA

PATHOLOGY

Inflammation.—Inflammation of the pleura is called pleuritis or more commonly *pleurisy* and when it is associated with an effusion into the pleural cavity it is known as *empyema*. Empyema is usually divided into two categories—pyogenic and tuberculous—because the treatment of the former is usually surgical while that of the latter is medical.

Pyogenic Empyema.—This type of empyema almost always follows pneumonia, influenza or measles, or is secondary to a pulmonary abscess, intrapleural hemorrhage, pulmonary infarction, subphrenic abscess, bronchiectasis, penetrating chest wounds, or operative procedure as diagnostic aspiration or aspiration biopsy. The *causative organisms* are pneumococcus in 75 per cent, streptococcus in 15 per cent and staphylococcus and Friedlander's bacillus in most of the remaining 10 per cent of the cases. There is no predilection for sex or age. *Symptoms* may appear insidiously, and consist of lassitude and shortness of breath, or they may be ushered in abruptly, and consist of a chill, septic temperature and pain in the side.

The *disease* affects both sides with equal frequency and may involve the entire pleural space as a single cavity (diffuse) or it may be walled off into one or more pockets (unilocular or multilocular). Both the visceral and parietal pleura are involved and the changes are those of inflammation. The surface becomes dull, rough, dry, thickened and hyperemic. Soon this is followed by an effusion into the pleural cavity to which are added fibrin, leukocytes and bacteria. The *pus* varies according to the offending organism.

Thus, in pneumococcal empyema it is thick and creamy with often a greenish tinge, in streptococcal it is thin, grey and watery, in staphylococcal it is thick, creamy or more yellowish, and in that caused by the Friedlander's bacillus it is thick, grey, mucoid and stringy. *Histologically*, the early changes consist of congestion of the submesothelial capillaries followed by a transudation of fluid and an escape of erythrocytes and leukocytes into the surrounding tissues. As a result the connective tissue becomes edematous and infiltrated with neutrophils and later plasma cells, lymphocytes, eosinophils and monocytes (Fig 154). The mesothelial cells



FIG 154

FIG 155

FIG 154—Empyema showing three zones—an inner of leukocytes and debris a middle of granulation tissue and an outer of fibrous tissue $\times 375$

FIG 155—Loculated empyema removed surgically. The walls are thick and fibrous. Clinically, this was mistaken for a carcinoma.

become tall cuboidal and as the infection progresses they slough into the pleural space. With a continuance of the inflammation there is a proliferation of both connective tissue and capillaries. The latter recede and disappear whereas the former, produced in abundance, becomes collagenous and causes a varied degree of thickening of the pleura.

Adhesions between the raw surfaces of the visceral and parietal pleura form early, and as the infection abates the pleuras become steadfastly glued together. If they become uniformly adherent the pleural space will later be entirely obliterated, but more often the adhesions are less diffuse and the intervening pleura will be

either restored to its normal luster or it may continue to occupy a pocket of pus or fluid. The latter may in time become surrounded by a dense fibrous tissue capsule and the entire mass may roentgenologically simulate a neoplasm (Fig. 155). Sometimes, however, the infection persists and the empyema passes to a *chronic*, smouldering stage. The *causes* of this are (1) attenuation of the infection, (2) inadequate drainage so that pus accumulates a little faster than it is drained, (3) fibrosis of the pleura and lung parenchyma both of which prevent the lung from re-expanding, (4) bronchopleural fistula and (5) the presence of foreign bodies as tubes, gauze, etc., in the pleural cavity.

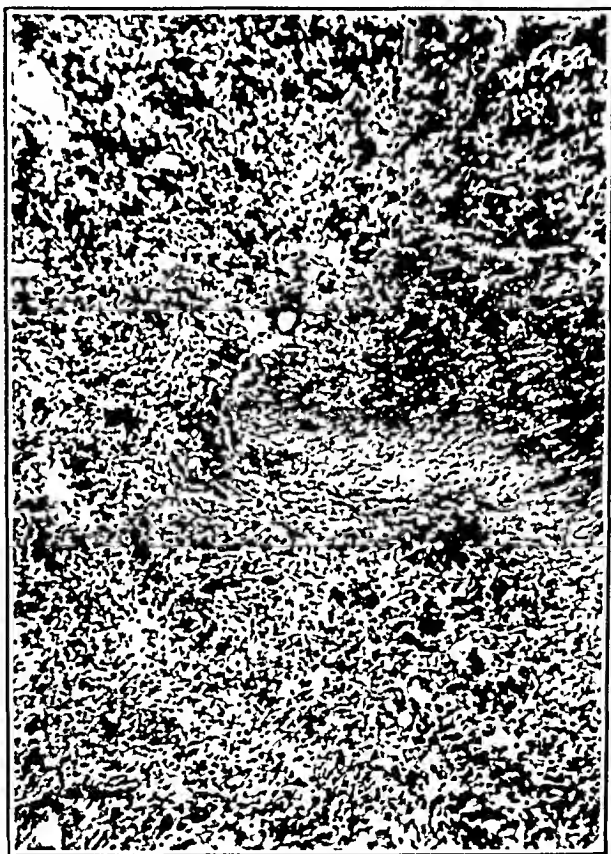


FIG. 156 —Tuberculous empyema. In the center and to the right there is an area of caseation necrosis surrounded by epithelioid cells. The rest is composed of connective tissue, capillaries, plasma cells and lymphocytes. $\times 100$.

The *treatment* of empyema, particularly that caused by the pneumococcus, streptococcus and staphylococcus is systemic and intrapleural administration of penicillin. Some patients will recover from this alone and in most of the others the empyema will become sterile. If the pus does not disappear, however, adequate surgical drainage must be instituted. Otherwise the empyema will become chronic or the *pus may burrow* into a bronchus, the trachea, esophagus, pericardium, mediastinum, large blood vessels and chest wall. The *prognosis* varies with the age. In infants under four months of age the mortality is about sixty-five per cent, whereas in adults it is only 6 per cent.

Tuberculous Empyema—Tuberculous empyema is always secondary to pulmonary tuberculosis and may arise spontaneously or more frequently as a complication of artificially induced pneumothorax. The fluid may be serous, serofibrinous, hemorrhagic or, with superimposed infection, frankly purulent. The initial lesions are seen only in uncontaminated tuberculous empyema. The pleura loses its normal luster, it may be quite hemorrhagic, and is frequently covered with a gelatinous or fibrinous exudate. Serosal tubercles are quite common along the anterior surface of the lung but are less frequent posteriorly. In time, the pleura becomes thickened by fibrous tissue and adhesions are formed. All the gross features are seen in histologic sections. The hemorrhagic appearance is due not so much to erythrocytic extravasation as it is to engorgement and dilatation of the subpleural capillaries particularly those around the tubercles. The latter as always consist of epithelioid cells with and without central areas of necrosis and peripheral giant cells, plasma cells and lymphocytes. Sometimes the submesothelial caseous pulmonary nodules are seen to perforate the pleura directly and thus empty their contents into the pleural cavity. Often, and particularly when there is an invasion with other organisms, the entire mesothelial surface is covered with *tuberculous granulation tissue* composed of caseating necrotic tissue, abundance of irregularly arranged epithelioid cells, few capillaries, fibrous tissue and varying numbers of plasma cells and lymphocytes (Fig 156). In such tissue the formation of discrete tubercles is usually not a prominent feature. The treatment of tuberculous empyema is medical, but repeated aspiration in the serous and hemorrhagic types is beneficial.

Tumors—Benign—Most benign tumors of the pleura are not ordinarily of much surgical significance because they are usually so small that they produce no symptoms and, as a rule, are found as incidental observations at autopsy. They arise from the submesothelial tissues and consist of fibroma, leiomyoma, lipoma, chondroma, neurofibroma and hemangioma.

Malignant—Although a malignant counterpart to each one of the benign tumors listed above has been recorded, such tumors of the pleura are not common. Only two will be considered here (1) giant sarcoma and (2) mesothelioma.

Giant Sarcoma—This is really not a tumor but several tumors, that arise from the visceral pleura and usually grow to giant proportions. They are not to be confused with giant cell sarcoma which is only one variety comprising the group. The tumors grow slowly and are present for many years before they produce symptoms. The latter are due entirely to pressure and result from compression of the lung, displacement of the mediastinum and heart, and obstruction to the circulation. Death frequently results from cardiac failure consequent to obstruction of the pulmonary circulation. Grossly, the tumors may be a few centimeters in diameter but more often they fill most or all of the hemithorax. They are all enclosed in a connective tissue capsule that is covered by a smooth membrane and this is continuous at the point of origin of the tumor with the pleura. Usually they are pedunculated and, secondarily, they may

become adherent to the diaphragm, parietal pleura, pericardium and other portions of the lung. *Histologically*, the tumors are quite bizarre and consist of round or spindle cells that resemble fibrosarcoma, irregular giant cells, embryonal connective tissue or fatty tissue. Despite their malignant microscopic appearance the growths rarely metastasize and for this reason they can be completely removed if the diagnosis is made early.

Mesothelioma.—The literature concerning mesothelioma of the pleura is still quite confused. The lesion has been described under at least 30 *different names* some of which are endothelioma, endothelial carcinoma, carcinoma, carcinosarcoma and mesothelioma. It is not a common tumor—its incidence being given as 0.02 to 0.2 per cent of all patients coming to necropsy. It occurs between the ages of forty to sixty years and is extremely rare in childhood.

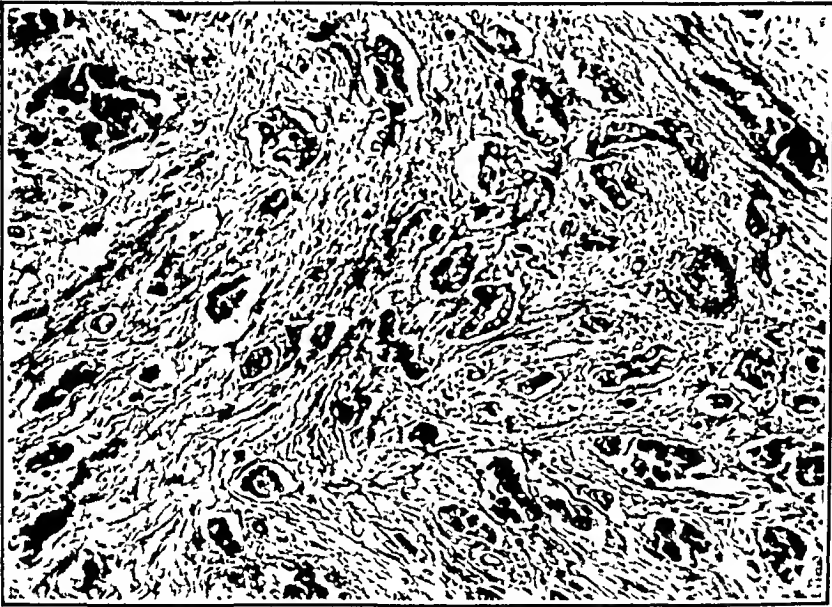


FIG. 157.—Mesothelioma of the pleura. Cuboidal cells in glandular formation are set in a dense fibrous tissue stroma x 100.

Males are affected twice as frequently as females. The *symptoms* develop gradually but occasionally the onset is that of acute pleurisy. Pain is the foremost complaint. It is gnawing in character, and at first is intermittent but later it becomes constant. This is followed by increasing dyspnea on exertion, dry cough, loss of weight, lack of energy and cyanosis. Although the tumor has been considered to arise from aberrant nests of pulmonary epithelium and from the endothelium of the subpleural lymphatics, it is now generally accepted that it originates in the mesothelium.

The *gross* features of the neoplasm are perhaps more characteristic than is its histologic structure. Each side of the thorax is affected with equal frequency. Usually by the time the lesion is discovered the entire pleura both visceral and parietal is replaced by a layer of firm pinkish grey or greyish white tumor that measures from 1 to 4 cm. in thickness. If the neoplasm is seen early enough, however, only a part of the pleura may be involved. The inner surface is

smooth but finely nodular, and the space between the visceral and parietal pleura is characteristically filled with a hemorrhagic fluid. The lung is practically never invaded, but the intercostal muscles are frequently infiltrated with tumor and the inner surfaces of the ribs are eroded. Although the *histologic* picture varies, the tumor usually discloses a marked desmoplastic reaction wherein the fibrous tissue contains few cells and much collagen (Fig 157). The disposition of tumor cells within this fibrous stroma is not uniform. They are arranged singly and diffusely, in sheets, cylinders, solid nests or definite alveoli. The latter are lined by a single layer of cells and the lumens are filled with desquamated and necrotic tumor tissue. The cells are round, spindle or polyhedral. The cytoplasm is moderate or abundant and is homogeneously acidophilic or basophilic. Occasionally, it is vacuolated. The nuclei are quite large and vesicular with a well-defined membrane and often containing distinct nucleoli. Giant cells are not common. Sometimes, there are present round bodies that are similar to corpora amylicia as seen in the prostate. Metastasis is infrequent, but secondary growths have been reported in the mediastinal lymph nodes and in almost all of the other organs and tissues of the body.

The *diagnosis* is made from the history, from a roentgenogram which shows a thickened pleura or a diffuse density, and from a thoracentesis at which time great resistance to the needle is noted when the pleura is reached and bloody fluid containing tumor cells is aspirated. There is no effective treatment. The *mortality* is 100 per cent.

Secondary growths of the pleura from primary foci in all organs and tissues of the body are common. The tumors reach the pleura by direct invasion from neighboring organs and tissues, by way of the blood stream and by way of the lymphatics. They are frequently accompanied by a pleural effusion which incidentally may be the only indication that something is amiss. The fluid may be straw colored but more often it is bloody. The centrifuged sediment when examined either by the paraffin method or by the Papanicolaou technique will disclose cancer cells in about 60 per cent of the cases. *Grossly*, the pleura may reveal a few scattered tumor nodules, numerous closely packed foci of varying sizes, or a diffuse thickening resembling a primary mesothelioma. *Microscopically*, the neoplasm resembles the parent growth.

Tumors of the Thoracic Inlet Producing the Pancoast Syndrome—This lesion can be defined as any tumor in the thoracic inlet that engulfs and destroys the brachial plexus and its branches, the cervical sympathetic trunk and the blood vessels, and that erodes the first and second ribs and the adjacent vertebrae and, in some cases, extends into the spinal canal. Consequently, it is accompanied by severe persistent pain around the shoulder and down the arm, a Horner's syndrome, swelling of the arm, face and neck, and, in the cases where the cord is destroyed, paraplegia. Although described over a hundred years ago, attention was forcibly directed to the syndrome by Pancoast in 1924. Since then it has been described under the following *varied names*, apico-costovertebral syndrome,

cancer of the thoracic pulmonary apex, superior pulmonary sulcus syndrome, sulcus tumor, primary apical lung carcinoma, extrapulmonary tumors of the thorax, sternoclavicular branchiomas, tumors of the superior thoracic inlet and Pancoast syndrome. It was Pancoast's opinion that he was dealing with a specific primary tumor but subsequently it has been shown that any tumor in the thoracic inlet can produce the syndrome.

Carcinoma of the lung accounts for two-thirds of the cases and metastatic tumors originating in all other organs of the body account for most of the remaining third. In addition, however, there are a few cases in which a primary site other than one in the thoracic inlet



FIG 158.—Primary bronchogenic carcinoma producing the Pancoast syndrome. The tumor occluded the bronchus to the left upper lobe producing bronchiectasis. Extension to the lymph nodes destroyed the left recurrent laryngeal nerve.

cannot be found and in these an origin in a branchial or bronchial rest has been postulated. In the recorded cases the lesion was found in 9 men to every 1 woman; the ages ranged from 16 to 73 years with an average of 48.6 years, and the duration of the illness from the initial symptoms to the time of death was 2 to 32 months with an average of 10.5 months.

Grossly, as stated in the definition, the tumor is located in the thoracic inlet, almost always involves the pleura, and surrounds or destroys all the vital structures at the base of the neck and in the thoracic inlet (Figs. 158, 159 and 160). One side is involved as often as the other. The neoplasm varies in size from 3 to 20 cm. or more. It is usually extremely firm, scirrhus, grey and lacks degeneration, necrosis or hemorrhage. The *microscopic* appearance varies according to the primary site but it almost always discloses a

marked desmoplastic reaction. Those tumors that originate in the thoracic inlet are composed of round, oval, or cuboidal cells with moderate acidophilic cytoplasm and are in anaplastic, glandular and squamous formation.

The diagnosis is made from the history in which is elicited pain in the shoulder and down the arm, from the physical examination which reveals a supraclavicular tumor and a Horner's syndrome on the affected side, and from the roentgenogram which discloses a mass in the thoracic inlet with often a destruction of the first and second

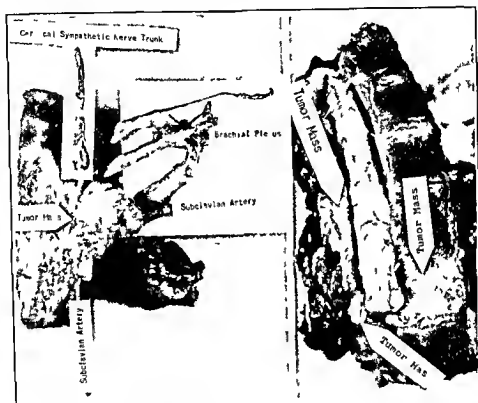


FIG 159

FIG 160

FIG 159—Same case as shown in Figure 158. The tumor is in the thoracic inlet where it engulfs the vital structures.

FIG 160—Same case as shown in Figure 158. The tumor has replaced the body of the first dorsal vertebra and has extended into the spinal canal producing paraplegia.

ribs and the corresponding vertebral bodies. Although both surgical extirpation and roentgen therapy have been tried, treatment is ineffective and the mortality is 100 per cent.

Mechanical Disturbances—Mechanical disturbances of the pleural cavity include (1) pleural effusion, (2) pneumothorax, (3) direct trauma and (4) foreign bodies.

Pleural Effusion—Pleural effusion means an accumulation of fluid in the pleural cavity beyond the normal 50 to 75 cc. *Empyema* has already been considered. There are three other types of effusion that deserve mention: (1) serous, (2) hemorrhagic and (3) chylous. A serous effusion (hydrothorax) frequently accompanies cardiac

failure, hypoproteinemia, Bright's disease, obstruction to the venous return to the heart and even carcinoma of the pleura. The fluid is straw colored, clear or cloudy, contains less than 3 per cent protein, does not coagulate spontaneously on standing, has a specific gravity of less than 1.018 and discloses only a few cells the majority of which are sloughed mesothelial cells.

An effusion is called *hemorrhagic* when the fluid is grossly bloody. The amount of blood varies from a trace to a frank recent or old hemorrhage, and the size of the effusion from 1 to 6 liters or more. Cancer of the pleura is responsible for 65 per cent of all cases of hemorrhagic pleural effusion, and the rest is accounted for by pyogenic pneumonias, tuberculosis, pulmonary embolism, fibroma of the ovary (Meig's syndrome), leukemia, uremia and cardiac failure.

A *chylous* effusion (chylothorax) is an accumulation of chyle in the pleural cavity. It is *caused* by any condition which produces a break in, or an obstruction to, the thoracic duct or its branches. More specifically, a break in its wall may be caused by trauma to the chest with or without fracture to the bony cage and, less frequently, by stab or gun-shot wounds, and injury at the time of operation. Obstruction to the thoracic duct is produced by compression of the duct from without by tumor or tuberculous nodes, by thrombosis of the left subclavian vein, by neoplasm of the duct itself, or by obstruction of the lumen with filaria. In infants chylothorax sometimes occurs without any apparent cause and it is attributed to a congenital weakness of the wall of the thoracic duct. The *diagnosis* is made from an examination of aspirated fluid. Chyle is milky, forms a creamy layer on the surface upon standing, is finely emulsified, ordinarily odorless, alkaline in reaction, has a specific gravity of over 1.012, is sterile and resists putrefaction. It is composed of 0.4 to 4.0 per cent fat, over 4 per cent total solids and over 3 per cent total proteins. *Treatment* consists of maintaining the nutrition of the patient by means of reinjecting the aspirated chyle with the hope that the continuity of the duct will re-establish itself. Plastic repair of the duct is usually unsuccessful. The *prognosis* is grave.

Pneumothorax.—Pneumothorax is defined as air in the pleural cavity. If the opening into the pleura acts as a valve air accumulates under pressure and the condition is then referred to as tension pneumothorax. The *source* of the air may be (1) from *without* as following trauma to the chest wall, during operations on the lung, after a tracheotomy or purposely induced as a therapeutic measure and (2) from *within* by escape of air from the lung. This usually starts as an interstitial pulmonary emphysema. Hyperventilation of the alveoli or a congenital defect in the alveolar wall causes a break in the surface and escape of air into the septum. The air follows the perivascular connective tissue (1) centripetally to the hilum of the lung and mediastinum whence it treks to the neck, retroperitoneal tissue, or through the pleura into the pleural cavity and (2) peripherally to reach the pleural cavity by direct extension through the visceral pleura. Another route for air from the lung is merely an overdistention of subpleural alveoli to form blebs which

later rupture directly into the pleural cavity. Hyperinflation of the alveoli frequently occurs during violent expulsive efforts resulting from laryngeal fractures, during parturition, following aspiration of foreign bodies, in asthma and accompanying pulmonary infections. Sometimes, however, the cause is less apparent and the over distension of the alveoli is then explained on the basis of areas of compensatory emphysema that accompany foci of atelectasis.

The signs and symptoms of pneumothorax consist of sudden pain in the chest, dyspnea, rapid pulse, shallow rapid breathing, hyperresonance and absence of breath sounds. A roentgenogram discloses air in the pleural cavity and collapse of the lung. The treatment is release of the air if it accumulates under tension, otherwise the patient is left alone. The prognosis in infants is poor, but in adults it is good.

Pneumothorax is always accompanied by atelectasis of the lung. In most cases in which the pneumothorax is accidental, and in 95 per cent of the cases in which it is therapeutic, when the air is resorbed the lung rapidly re-expands. In some of the former and in 5 per cent of the latter, however, the lung becomes *unexpandable*. The causes for this are (1) massive fibrosis of the lung parenchyma consequent to healing of large tuberculous cavities or to non-specific pneumonitis, (2) pleural fibrosis, (3) pleural adhesions and (4) bronchopleural fistula.

Direct Trauma—In civilian life trauma to the chest wall, pleura and lungs is not too common but in battle it is of frequent occurrence. The injuries sustained may be listed as (1) those involving the thoracic cage such as bruises, lacerations, fractures, etc., (2) those involving the pleural cavity which include hemopneumothorax, clotted hemothorax, tension pneumothorax and empyema and (3) those involving the lung which consist of contusion, laceration and pulmonary abscess. The mortality rate in battle wounds of the thoracic cavity has been only 7 per cent.

Foreign Bodies—Intrapleural foreign bodies in civilian life are not common but in warfare they are frequent. Their importance lies in the fact that they are usually accompanied by a chronic *empyema*. They may be divided into those gaining entrance by *inhalation* and those gaining entrance by *penetration* through the chest wall. The former include straw, grass, rye, barley and other grain ears and artificial teeth, whereas the latter include wood splinters, missiles from fire arms and surgical material such as broken needles, rubber drainage tubes, gauze and masses of zinc oxide ointment.

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Chapter VI

NECK

THYROID GLAND

EMBRYOLOGY

THE main portion of the thyroid gland originates in the 2 mm embryo as a midline evagination of the pharyngeal entoderm at the level of the first pouch. It soon becomes a solid mass that lies at the level of the aortic trunk and is attached to its point of origin by a narrow neck known as the thyro-glossal duct. By the fifth week the latter disappears except for a small depression at the base of the tongue called the foremen caecum. Shortly thereafter, the mass assumes a transverse position with a lobe on each side of the trachea, and at the seventh week it becomes fused with the rudimentary fifth pouches—the ultimobranchial bodies—which are subsequently transformed into thyroid tissue. In the eighth week the entire mass is converted into plates and cords, and these in turn become hollow, acquire colloid and thus form acini or follicles. Transformation of the primitive mass into follicles ceases during the fourth embryonic month, after which new follicles arise only as a result of budding from existing acini.

ANATOMY

The normal thyroid gland is located in the anterior portion of the neck opposite the fifth, sixth and seventh cervical vertebrae. Its total weight is approximately 30 gm. It is composed of a right and a left lateral lobe, an isthmus and, frequently, a pyramidal lobe. Each lateral lobe measures about $5 \times 3 \times 3$ cm. It is conical in shape with its apex at the level of the middle and lower third of the thyroid cartilage and its base at the level of the fifth or sixth tracheal ring, and it is enveloped by a fascial sheath derived from the pre-tracheal layer of the fascia colli. The posterior and medial portion of each lobe is attached to the cricoid cartilage and is moulded over the larynx and the trachea, whereas the posterior and lateral surface overlaps the common carotid artery. The isthmus is 1.25 cm long and 1.25 cm broad, it covers the second, third and fourth tracheal cartilages, and it connects the lateral lobes. A third or pyramidal lobe often extends superiorly from the isthmus or the medial portion of one of the lateral lobes to the hyoid bone. The arterial supply to the thyroid gland comes from the superior thyroid artery (which arises from the external carotid), from the inferior thyroid artery (which arises from the thyrocervical trunk of the subclavian), and from the thyroidea ima artery (which arises from the innominate artery or from the arch of the aorta). The veins form a plexus which emerges as a superior and middle thyroid vein that empty into the external jugular vein, and an inferior thyroid vein that empties

into the innominate vein. The *lymphatic* vessels are disposed about the arteries and drain into the thoracic and right lymphatic ducts.

Histologically, the thyroid gland is covered by a double capsule—an external one connected with the cervical fascia and an internal one intimately bound with the gland itself. The parenchyma is composed of aggregations of follicles separated by strands of connective tissue. The follicles are lined with a single layer of cuboidal epithelial cells in portions concerned with the production of thyroid hormone and with tall columnar epithelium in areas concerned with resorption of the hormone (Fig. 161). Their cytoplasm contains

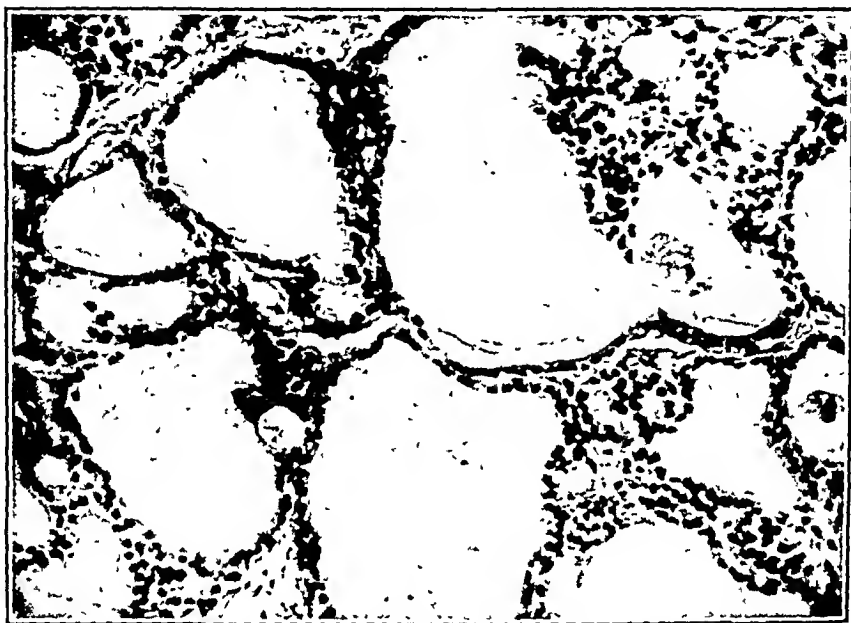


FIG 161.—Normal thyroid gland. The acini are filled with dense colloid and are lined with cuboidal cells x 200.

short thin rod shaped bodies—the mitochondria. These are most numerous between the nucleus and the lumen, are not seen in ordinary hematoxylin and eosin stained sections, and are doubtlessly concerned with the formation of secretion. The lumen of the follicle is normally filled with iodine containing colloid. In the fresh gland, colloid is clear and viscid while after fixation it is solid and stains deeply with eosin. Vacuoles that are often found between the colloid and the epithelium are held by some to be evidence of resorption and by others they are considered as artefacts. The external surface of the cuboidal cells forming the follicles rests not upon a basement membrane but upon loose connective tissue which contains blood vessels, lymphatics, nerves, few lymphocytes and scattered macrophages.

PHYSIOLOGY

The thyroid is an important ductless gland that is regulated by the pituitary gland and is closely connected with the sex glands. Its two most obvious functions are to regulate the metabolism of the body and to promote physical and mental growth. In adults if the

gland is *overactive* it results in an increase of metabolic activities (see hyperplasia below) while if it is *underactive* it produces *myxedema* (subnormal temperature, slow pulse, clumsy gait, coarse hair, thick dry skin, broad face, thick lips and tongue, intolerance to cold, irregular menses, gain in weight and low basal metabolic rate). Underactivity in infants results in *cretinism* (dwarfed stature, clumsy gait, pendulous abdomen, coarse hair, dry skin, round full face, enlarged tongue, harsh voice, undeveloped secondary sex characteristics, and severe mental retardation). Symptoms of hypothyroidism both in adults and in infants can be completely controlled by the administration of *thyroxin*—the active hormone secreted by the thyroid gland. Although it is known that thyroxin is manufactured by the epithelial cells, that iodine is a necessary prerequisite for its formation, and that it is stored in the alveoli in the form of colloid, the exact mechanism or mechanisms involved in its production are not clearly understood.

PATHOLOGY

Congenital Anomalies—Developmental abnormalities of the thyroid gland consist of hypoplasia, aplasia, lingual thyroid, aberrant thyroids, thyroglossal cysts and sinuses, and parathyroid and thymic inclusions. Congenital hypoplasia produces infantile myxedema and aplasia results in cretinism. Both of these are medical problems. Of surgical importance are lingual and aberrant thyroids and abnormalities of the thyroglossal duct. These will, therefore, be considered in more detail.

Lingual Thyroid—As the name implies this anomaly consists of a persistence of a part or all of the thyroid at its point of origin, namely, the base of the tongue or the foramen caecum. Although it is truly a congenital lesion only a few cases are recognized at birth whereas the majority are detected at puberty and during pregnancy—at a time of maximum physiological enlargement of the thyroid gland. Other factors responsible for its increase in size are physiological or artificial menopause, thyroidectomy, and destruction of the thyroid gland by inflammatory or neoplastic pathologic processes. Over three-quarters of all reported cases are females. *Symptoms* may be entirely absent or, when the lesion gets large enough, they may consist of difficulty in speaking, breathing and swallowing, of pain, cough, feeling of fullness, and a desire to swallow. Hemorrhage occurs in 10 per cent of cases as a result of trauma, ulceration or infection, cretinism is reported in an equal number of cases, and hyperthyroidism is most unusual.

The *lesion* is single, located in the midline in the region of the foramen caecum, measures a few millimeters or 6 cm or more in diameter, is raised, pedunculated or sessile, has a smooth or lobulated and intact or ulcerated surface, is pink or deep red in color, and is firm, solid, elastic or cystic in consistency. *Histologically*, it usually resembles a normal thyroid although, occasionally, it is the seat of an adenoma and, rarely, it undergoes a carcinomatous change.

Treatment consists of surgical excision provided there is functioning thyroid tissue in the normal location. The indications for operation are embarrassment to speaking, swallowing or breathing, repeated or severe hemorrhage, hyperthyroidism, and suspected carcinomatous transformation. The *prognosis* is good.

Lateral Aberrant Thyroids.—Aside from lingual thyroid aberrant thyroid tissue may be found at any point along the midline between the base of the tongue and the mediastinum, within the trachea, and laterally in the neck. The latter deposits are of particular interest because they offer difficulty in diagnosis, because they are not rare, and because their genesis is not agreed upon. A minority of observers contend that any detached thyroid tissue lateral to the main mass represents a *metastatic carcinoma* from the homolateral lobe of the thyroid, whereas a majority of writers consider such deposits as embryonal rests. Doubtlessly, both views are correct. Apart from metastases lateral aberrant thyroids can be readily explained on a *developmental* basis. It has been pointed out in the opening paragraph of this chapter that the thyroid gland develops from a midline evagination of the pharynx and from the last pharyngeal pouches—the ultimobranchial bodies. When the latter fail to unite with the main mass, they may remain high up in the lateral portion of the neck or they may be dragged inferiorly by the thymus as low as the mediastinum. Thus thyroid tissue developing from these pouches may be found beneath the sternocleidomastoid muscle anywhere along the chain of deep cervical lymph nodes. The three most common *sites* are (1) above the omohyoid muscle, (2) below the omohyoid muscle and (3) in the supraclavicular area. Although congenital in origin the nodules usually do not become apparent until beyond the fourth decade of life but one of our cases was in a boy seven years old. They are found in females more frequently than in males, and are often of many years duration. *Symptoms*, if present at all, consist only of a swelling in the lateral portion of the neck. As such the lesion must, therefore, be *differentiated* from lymphadenitis, tuberculosis, lymphoblastomas, metastatic carcinoma, branchial cysts and carotid bodies.

Grossly, the nodules vary in size from that of normal lymph nodes to a diameter of 6 or 8 cm. or more. They may appear homogeneously beefy red or encapsulated, adenomatous and cystic. *Histologically*, they are usually seen to be embedded in lymphoid tissue and may appear as normal or diseased thyroid tissue. They have a tendency to become cancerous in which instance they cannot be distinguished microscopically from primary carcinoma of the thyroid proper that has metastasized to the cervical lymph nodes. *Treatment* consists of local excision of the nodules when they are benign, and of a radical dissection when they are malignant. The *prognosis* in the former is good while in the latter it depends entirely upon whether the disease is localized or already disseminated. Frequently, there are local recurrences and ultimately, the patients die from metastases.

Thyroglossal Cysts, Sinuses and Fistulas.—Thyroglossal cysts may occur anywhere along the course of the thyroglossal duct, but

are most common below the hyoid bone. When they present one opening to the exterior (less commonly at the base of the tongue and more often in the skin covering the midline of the neck) they are referred to as *sinuses*, and when they are open at both ends they are called *fistulas*. They are found at all ages from birth to sixty years or more, and affect both sexes with approximately equal frequency. In eighty-five per cent of cases the anomaly is a *cyst* that varies in size from a few millimeters to 4 cm. in diameter with an average of 1 to 2 cm. It is found in the midline, is smooth and round, has well-defined borders, is not tender unless it is infected, and when small it moves freely in all directions. It is almost always attached to the deeper structures, particularly to the hyoid bone, but not to the skin. The sinus opening is usually in the midline between the hyoid bone and the suprasternal notch. It measures 1 to 3 mm. in diameter, is surrounded by chronic inflammation and exudes clear, mucoid or purulent fluid.

Histologically, the inner surface is covered with pseudostratified ciliated or non-ciliated columnar and, occasionally, with stratified squamous epithelium (Fig. 162). The lining may be smooth or



FIG. 162.—Thyroglossal duct lined with pseudostratified ciliated columnar epithelium
x 200

it may project laterally in the form of small blind pockets. Sub-epithelially, there is a varied degree of infiltration with neutrophils, plasma cells and lymphocytes and beyond this the tissue is dense and fibrous. Microscopically, the tract is usually seen to extend through the center of the hyoid bone and into the tissue between the latter and the base of the tongue even in those cases in which close gross inspection and careful probing fail to reveal its presence. In a differential diagnosis there should be considered submental lymphadenitis, tuberculous sinus tract from the mediastinum, lipoma, dermoid or sebaceous cyst and an ectopic thyroid. If the

cyst is not large, if it produces no disfigurement and if it is not infected it should be left alone otherwise it should be *excised*. All sinuses and fistulas should be removed because they are prone to infection. Any extirpation is not considered adequate unless the central portion of the hyoid bone and the entire tract to the foramen caecum is removed. If treated in this manner there should be no recurrences.

Inflammation.—The thyroid gland is singularly resistant to infection of any kind due doubtlessly to its anatomic structure. Externally, it is guarded by heavy muscles and fascia and is enveloped by a stout capsule. Internally, it contains no duct which would convey infecting agents; it is supplied with lymphatic vessels that are provided with effective valves; it is furnished with an overabundance of arteries, and it possesses good venous drainage. It is axiomatic, therefore, that an infected thyroid gland was previously not normal. Some of the factors predisposing to thyroiditis are: adenoma, hyperthyroidism, physiological hyperplasia as seen at puberty, menstruation and pregnancy, and prolonged fevers and other debilitating diseases. The inflammations may be divided into acute, chronic non-specific and chronic specific.

Acute Thyroiditis.—Acute infection of the thyroid gland is commonly divided into acute *non-suppurative* and *acute suppurative*. The former is probably bacterial in origin but since it is transitory and usually resolves in from seven to ten days, little is known with regard to both its causative agent and to the pathologic changes. Since the cases that ultimately do form abscesses are initially the same as those that do not, it is reasonable to assume that suppurative thyroiditis is merely a progression of the non-suppurative type. *Organisms* most commonly isolated from the latter are streptococcus, staphylococcus, pneumococcus, typhoid bacillus and paratyphoid bacillus. Infection reaches the thyroid most frequently by blood stream metastases and rarely by penetration from the outside (in cases of trauma), by contiguity from adjacent tissues and by way of the lymphatic vessels. Some of the precise predisposing infections are influenza, pneumonia, pharyngitis and tonsillitis, puerperal fever and rheumatic fever. The disorder affects females twice as frequently as it does males, and it occurs most often between the ages of twenty to forty years with extremes of seventeen months and seventy-seven years. *Symptoms* consist of pain, swelling and tenderness over the thyroid with or without chills, fever, cough, dyspnea and dysphagia. The patient is usually in the sitting position with the head flexed, for this is associated with the least discomfort. The thyroid gland is diffusely or asymmetrically enlarged or the swelling may occupy the entire area between the hyoid bone and the sternum. The overlying skin may be warm, red and fixed if the abscess is situated anteriorly. Otherwise it is unaffected.

Pathologically, the outlines of the thyroid gland may be obscured by an associated edema. Sections may reveal abscesses limited to one lobe or the isthmus, evidence of pre-existing disease, as for example, adenomatous hyperplasia, or merely a diffuse induration. *Histologically*, there are dilatation and proliferation of capillaries,

hemorrhagic extravasation in the interstitial tissue and acini, a diffuse infiltration with neutrophils and lymphocytes, a diminution or complete disappearance of colloid and its replacement with granular precipitate, and fibroblastic proliferation. The acute process then recedes and resolves, or it progresses to the formation of abscesses or gangrene.

The *diagnosis* is established on a clinical basis for a diagnostic biopsy is not justified. In a differential diagnosis one should consider physiological hypertrophy, hemorrhage and cancer of the thyroid gland, and a phlegmon in the neck. *Treatment* is symptomatic, chemotherapeutic and, when suppuration is present, surgical drainage. *Complications* are perforation into the larynx or the trachea, mediastinitis, pyemia, myxedema and thyrotoxicosis.

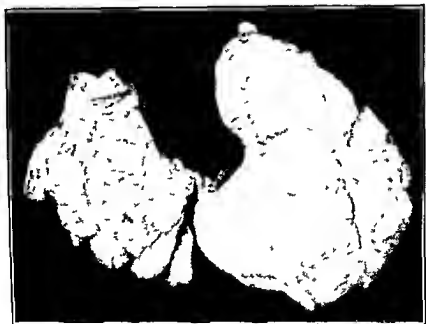


FIG. 163—Riedel's struma approximately natural size

The *prognosis* in non-suppurative cases is excellent, whereas in suppurative cases, although recovery is frequent, it is marred by a stormy convalescence.

Chronic Non-specific Thyroiditis—Only two disease processes of the thyroid gland will be included in this category—Riedel's struma and struma lymphomatosa. Although the latter is not, strictly speaking, an inflammatory disorder it is considered here simply because it has often been associated with, and frequently discussed in conjunction with, Riedel's struma.

Riedel's Struma—This disease first described by Riedel in 1896 is also called chronic thyroiditis and ligneous (woody) thyroiditis. Its cause is unknown. It is estimated that its incidence in all patients submitted to thyroidectomy is approximately 0.36 per cent. It occurs most often between the ages of twenty and sixty years with an average of fifty-one years, it attacks both men and women

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Clinically, there is nothing to absolutely distinguish Riedel's struma from carcinoma of the thyroid gland and the diagnosis is, therefore, usually made histologically. Treatment consists of surgical extirpation of enough of the gland to relieve pressure. Post-operative hypothyroidism develops in about 25 per cent of the cases which, of course, can be controlled by administration of thyroxin. The ultimate prognosis is good.

Struma Lymphomatosa—This condition is also referred to as Hashimoto's disease or Hashimoto's struma. It is confined to women around the age of fifty years. The chief complaint is gradual enlargement of the thyroid gland over an average period of fifteen months with extremes of from a few days to thirty years or more. Symptoms of pressure upon the trachea and esophagus develop in a few cases, nervousness is found only occasionally, the basal metabolic rate is either normal or slightly below normal, and evidences of hypothyroidism are present in a minority of patients when they are first seen. Examination discloses a diffuse uniform or nodular enlargement of the thyroid in 100 per cent of the cases, the patients are moderately obese, there is a slight relative lymphocytosis, and at operation the thyroid gland is found to be adherent only to the trachea.

Grossly, the boundaries of the gland are clearly defined, the surface is smooth or lobular, and the entire organ has weighed from 17 to 340 gm with an average of 91 gm. The capsule is well-defined but not thickened. Cut surfaces are dense, homogeneous, traversed by bands of fibrous tissue and vary in color from grey to white, pink or brown (Fig 165). The consistency is hard, firm or soft. The outstanding histologic change is lymphoid infiltration either in the form of single cells or well-defined follicles with active germinal centers (Fig 166). Sometimes the lymphoid tissue is moderate in amount but at other times it almost completely replaces the entire parenchyma. The acini tend to group together, are depleted of their colloid, and are usually small, although a few may be hyperplastic. As a rule most of the cells are low or tall cuboidal and their cytoplasm is dull and granular, but some are larger, have an abundant pale eosinophilic cytoplasm and are identical with the so-called Hurthle cells. Connective tissue is rarely prominent, the vascularity is normal or moderately increased, plasma cell infiltration is not conspicuous, and at times giant cells are seen grouped around small collections of colloid.

A diagnosis of struma lymphomatosa is ordinarily made histologically for there is nothing distinctive in the history or physical examination. But even a microscopic diagnosis may be confused with hyperthyroidism in which there is considerable lymphoid infiltration. Treatment of choice is subtotal thyroidectomy, although this is attended with post-operative myxedema in over forty per cent of cases. Since lymphoid tissue responds to roentgen irradiation, this form of therapy has been advocated, but the difficulty lies in the fact that the diagnosis is not made as a rule until after the gland has been extirpated. Except for consequent hypothyroidism the prognosis is good.

with almost equal frequency, and its onset is insidious although once symptoms become manifest, they are rapidly progressive. The most common *complaints* are dyspnea, dysphagia, dysphonia, pain, tenderness and, occasionally, symptoms of hyperthyroidism. The basal metabolic rate is usually normal. Examination discloses a diffuse, irregular, or unilateral stony hard involvement of the thyroid gland with fixation to all the adjoining structures except the skin.

Grossly, the gland is slightly larger than normal (Fig. 163). In early cases it does not differ greatly from ordinary hyperplasia. Later the external surface is ragged; the capsule is thick and fibrous; the involved portion is hard or woody in consistency, white, cuts with difficulty leaving a finely granular or lobulated surface, and it may or may not contain areas of adenoma.



FIG. 164 —Riedel's struma showing severe fibrosis and atrophy of acini. x 100

Histologically, the dominant feature is fibrosis (Fig. 164). In early cases the fibrous tissue is cellular and is increased both interlobularly and intralobularly. Later it becomes hyalin and replaces most or all of the parenchyma. The acini gradually become smaller and the colloid is rapidly absorbed. That which does remain is either granular or watery. The epithelial cells of the alveoli are normal, tall columnar (with granular eosinophilic cytoplasm), low cuboidal, or degenerated and in various stages of disintegration. Frequently, they are collected into small foci and when they surround small deposits of colloid or debris they may be mistaken for Langhans' giant cells. It should be pointed out, however, that true giant cells are also sometimes present. A diffuse infiltration with lymphocytes and definite lymph follicle formation are frequently encountered in early lesions but are less numerous in older cases. Plasma cell infiltration is always seen in varying degrees.

from adjacent structures particularly lymph nodes. Although tuberculosis has been demonstrated in other organs only occasionally, it is probably that all cases are secondary to foci elsewhere in the body. Treatment has consisted of partial thyroidectomy because of a mistaken diagnosis, or of incision and drainage in cases of abscess formation. Healing in the latter is delayed, but the prognosis in all cases is good provided there is no demonstrable lesion elsewhere.

Tumors—For all practical purposes tumor formations of the thyroid gland are limited to epithelial overgrowths. On rare occasions, however, other tissues participate and accordingly the following histogenetic classification is applicable from epithelium there develop such benign processes as diffuse colloid goiter, diffuse



FIG. 167.—Diffuse colloid goiter. The acini are filled with dense colloid and are lined with flat epithelial cells. $\times 100$

hyperplasia and adenoma and the malignant counterpart—carcinoma, from connective tissue fibroma and fibro-sarcoma, from blood vessels endothelial sarcoma, from lymphoid tissue lymphosarcoma and Hodgkin's disease as a result of metaplasia of mesodermal elements osteoma, chondroma, osteosarcoma, osteochondrosarcoma and plasmacytoma, from nervous tissue melanoblastoma, from mixed tissues teratoma, and finally, exogenous malignant tumors reaching the thyroid either as a result of metastasis or direct extension. Only the epithelial overgrowths and the latter are encountered frequently enough to warrant further elaboration.

Diffuse Colloid Goiter—The term goiter is used to connote any enlargement of the thyroid gland, and the terms diffuse colloid merely signify a widespread infiltration with colloid. This lesion is endemic in districts where drinking water has a low iodine content, is particularly prevalent from prepuberty to late adolescence and in pregnancy, affects females more frequently than it does males,

Chronic Specific Thyroiditis.—Granulomatous lesions of the thyroid gland are rare. *Tertiary syphilis*, both diffuse and gummatous, has been reported but is most uncommon. *Tuberculosis* is more frequent. Its incidence is approximately 0.1 per cent of all surgically removed thyroids; it affects women four times as frequently as it does men, and is found between the ages of twenty and sixty years. In the reported cases tuberculosis of other organs was present in less than ten per cent of cases and most of these were instances of pulmonary infection. *Symptoms* may consist of any of the following: slowly

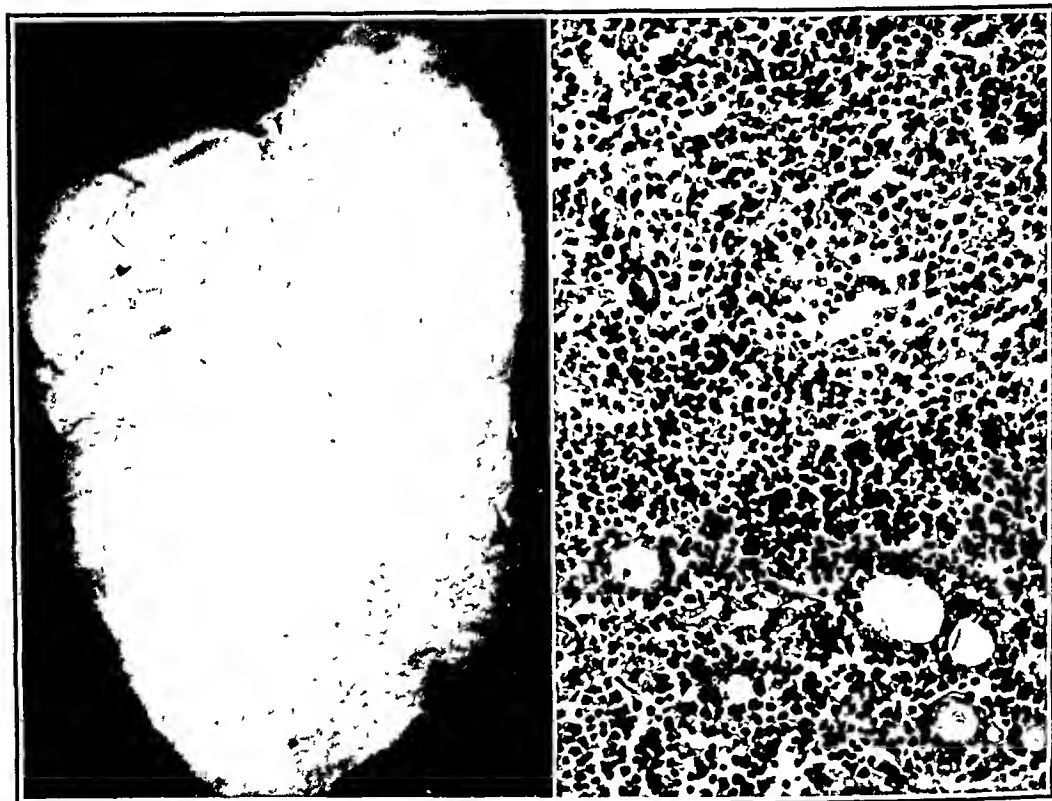


FIG 165.

FIG 166

FIG 165 —Struma lymphomatosa. The cut surface is light brown and has the appearance of a greatly enlarged lymph node

FIG 166 —Struma lymphomatosa illustrating a massive infiltration with lymphoid cells and atrophy of acini x 100

increasing mass in the neck of a few days to several months duration, slight pain and tenderness over the thyroid gland, dysphagia, dyspnea and manifestations of hyperthyroidism. The gland is usually only slightly enlarged, firm and smooth, although it may contain a fluctuating swelling. *Histologic* changes are those of tuberculosis in any tissue or organ. Tubercles are found between or within the acini. They may be small and miliary or large and conglomerate with central areas of caseation. Progression of the latter will result in complete breaking down of tissue and abscess formation whereas regression will be attended by fibrosis. The *causative organism* is the tubercle bacillus and it gains access to the organ by way of the blood stream, the lymphatics or by contiguity

is intact, the external surface is reddish brown and finely pebbled, and the consistency is firm. In patients not receiving any pre-operative iodine therapy or in those treated with thiouracil alone, cut surfaces are rather dull and diffusely light brown to deep reddish brown (Fig 168). They are frequently and aptly likened to a piece of beefsteak. In patients who have been treated before operation with Lugol's solution, the typical beefy appearance is replaced with a glistening, somewhat transparent sheen, the degree of which depends upon the amount of involution. Occasionally, a



FIG 169

FIG 170

FIG 169—Diffuse hyperplasia of thyroid gland showing acini devoid of colloid and lined with columnar epithelium $\times 100$

FIG 170—Diffuse hyperplasia of thyroid gland showing involution consequent to iodine therapy $\times 100$

small adenoma may be buried in a hyperplastic gland. The histologic structure likewise varies according to the preoperative medication. In the absence of Lugol's solution or thiouracil, the acini are large, round, oval or irregular, disclose papillary infoldings of epithelium into the lumens, and are empty or contain varied amounts of pale staining, granular or watery colloid (Fig 169). Most of the lining cells are tall cuboidal, loosely packed, bulge into the lumen and have irregular inner borders. The cytoplasm is lightly stained, granular or vacuolated and the nuclei are usually basilar in position and frequently in a state of mitosis. The supporting stroma is as a rule scanty, vascular and contains a sprinkling or a dense infiltration with lymphocytes. Frequently,

and can be ameliorated or prevented by the administration of potassium iodide or thyroxin. With the more widespread use of iodized salt in cooking, the disease in the United States is decidedly less common than it was formerly, and since it is a deficiency disorder the pathologist rarely has the opportunity to study a surgically removed specimen. The *thyroid gland* is diffusely but some times irregularly enlarged. It may be of moderate size or it may be enormous, filling the entire space between the chin and the sternum. It is well-encapsulated, moderately firm or soft and on section presents a grey or brownish vesicular, honeycombed, glistening, gelatinous surface. In some cases an irregular and massive enlargement

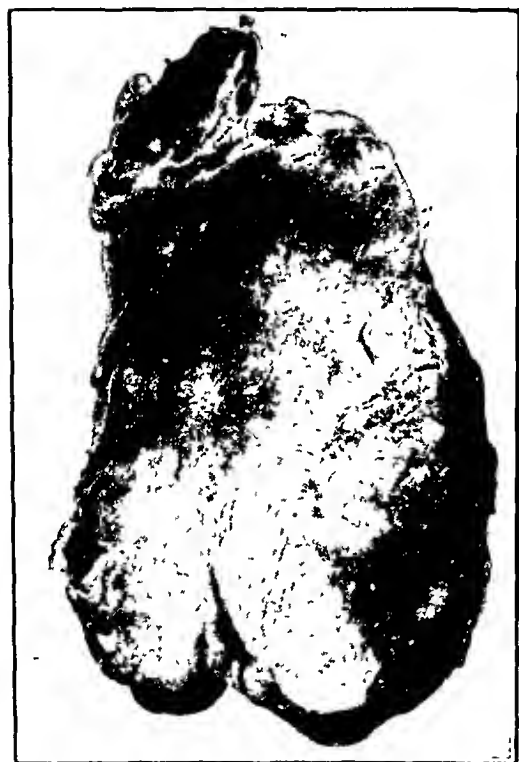


FIG 168.—Diffuse hyperplasia thyroid gland—one lobe of approximately natural size

of a group of acini with some compression of surrounding alveoli eventuates in an adenomatous appearance, and degeneration of the central portion of these masses may result in complete liquefaction and even secondary hemorrhage. *Histologically*, the acini vary considerably in size but, generally, they are large and some times huge (Fig. 167). They are lined with cuboidal or flattened epithelium and are filled with pale, acidophilic, thin colloid.

Diffuse Hyperplasia.—Diffuse hyperplasia of the thyroid gland is purely a pathologic term used to indicate a general increase in size of the gland attended by symptoms of hyperactivity. The clinical *synonyms* are exophthalmic goiter and Graves' disease. It results from an excessive stimulation of the thyroid parenchyma by the pituitary gland, but the exact cause of this is not known.

An important predisposing factor is a nervous temperament coupled with a severe illness, mental strain, shock, fright and grief. It affects females three or four times as frequently as it does males, often has an abrupt onset, and is most common between the ages of twenty and forty-five years. Five of the most important *symptoms* are goiter, nervousness and irritability, tremors, tachycardia, and palpitation, and the most important laboratory aid is an increased basal metabolic rate. There may also be exophthalmos, loss of weight despite a good appetite, dyspnea, cardiac decompensation, increased perspiration and flushing, intolerance to heat, emotional instability, weakness, fatigue, fever, diarrhea and scanty menstruation.

Grossly, the gland is either normal in size or only moderately enlarged. The average weight is between 40 and 50 gm.; the capsule

diameter and protrude anteriorly beneath the skin, posteriorly behind the trachea, or inferiorly into the mediastinum. They are firm, hard, soft or cystic and they usually show no fixation to the surrounding structures.

Grossly, the findings at physical examination are usually borne out. The nodules are single or multiple, as a rule they weigh between 20 and 200 gm., and they frequently measure 2 to 6 cm. in diameter. Externally, they are irregular, sharply circumscribed and usually well encapsulated. The capsule may be thin and deli-



FIG 171

FIG 172

FIG 171 —Fetal adenoma of the thyroid revealing a moderate degree of hemorrhage

FIG 172 —Colloid adenoma of the thyroid disclosing cystic degeneration

cate or rather broad, dense and fibrous. It often sends trabeculae into the nodule and sometimes it contains yellowish foci of necrosis and irregularly circumscribed areas of calcification. The enclosed parenchyma may be solid, dull and beefy red or it may be glistening and semitransparent. Often it presents a variegated appearance with alternating areas of light brown, beefy red, grey and yellow (Fig 171). At other times the entire mass is necrotic, cystic and replaced with clear or hemorrhagic fluid or it may become partly or completely calcified (Fig 172). *Histologically*, the surrounding thyroid parenchyma is usually compressed. The capsule is as a rule composed of dense acellular fibrous tissue and it frequently contains foci of lymphocytes, hemosiderin, calcium and cholesterol

the latter form lymph follicles with definite germinal centers, and sometimes these may be so abundant as to render the microscopic sections indistinguishable from those of struma lymphomatosa. Preoperative administration of *thiouracil* merely intensifies the aforementioned hyperplasia, whereas treatment with *Lugol's* solution eventuates in involutionary changes. These consist of a re-accumulation of abundant, densely eosinophilic, vacuolated and scalloped colloid, of concomitant disappearance of papillary infoldings, and of a return of most of the epithelial cells to a flat or low cuboidal variety (Fig. 170). In some areas the septums become thin or even break down completely leaving circumscribed groups of dilated follicles which in reality are just one step away from colloid adenoma.

A clinical *diagnosis* of diffuse hyperplasia of the thyroid is arrived at from the history and physical examination as already outlined, and an increased basal metabolic rate. The only permanently effective *treatment* is thyroidectomy, and this is a relatively innocuous procedure only if the patients are properly prepared beforehand. Preoperative treatment consists of increased caloric intake, conservation of energy, reduction of psychic trauma, reassurance, treatment of complicating diseases or infections, and the administration of thiouracil followed by iodine. Patients are ready for operation when they have gained weight, when the resting pulse rate is below 100, when the basal metabolic rate is below 50, and when they have responded to thiouracil and iodine. It should be pointed out, however, that *thiouracil* is not entirely harmless for its use in a series of about 6000 treated patients has resulted in the following *complications*: death in 0.5 per cent of cases, agranulocytosis in 1.8 to 2.5 per cent, leukopenia in 3.0 to 4.4 per cent, fever 2.7 to 5 per cent, and skin reactions in 3.3 per cent. Failure to prepare the patient properly may result in what has been termed post-operative "thyroid crisis"—a progressive augmentation of all the symptoms of toxicity with a breakdown of the central nervous, cardiovascular, hepatic or renal systems, and frequently terminating in death. Generally speaking, the *prognosis* is good although in a few patients symptoms of hyperthyroidism recur necessitating a second operation.

Adenoma.—In this category will be included any nodular enlargement of the thyroid gland that is not carcinomatous. Like diffuse colloid goiter these lesions are most common in goitrous districts, but the proportion of the former to the latter varies greatly. They affect women seven times as frequently as they do men, and, although they are found in infancy and childhood, they are decidedly more common after the age of twenty-five years. In one-half of the cases the only *symptom* is a mass in the neck, whereas in the remaining half there are some or all of the symptoms of toxicity that have already been enumerated in the preceding section on diffuse hyperplasia. Hoarseness, dyspnea and dysphagia are infrequent. Physical examination discloses an involvement of any or all of the lobes of the thyroid gland by a single or by multiple nodules. They vary in size from barely perceptible to 10 cm. in

is the most common. It consists of large, small and intermediate acini filled with dense, intensely eosinophilic colloid (Fig 175). The lining cells are usually flat cuboidal, although they may be cuboidal or less frequently columnar. The amount of cytoplasm, therefore, varies accordingly, but the nuclei are always round or

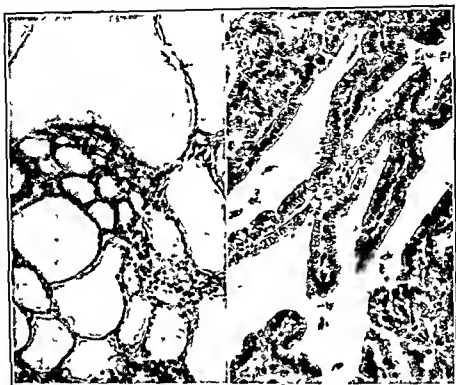


FIG 175

FIG 176

FIG 175—Colloid adenoma showing small and intermediate acini filled with dense colloid and lined with flat epithelium $\times 100$

FIG 176—Papillary adenoma. Thin stalks of connective tissue are covered with a single row of tall cuboidal cells. There is no colloid $\times 100$

oval, of uniform size and evenly stained. About the periphery of the colloid-filled acini there are often newly formed daughter alveoli that are considerably smaller and contain varying amounts of colloid. *Papillary adenoma* is also called *papillary cystadenoma*. The acini are large and contain numerous long slender finger-like infoldings (Fig 176). Their stalks are composed of thin strands of well-vascularized loose connective tissue. The covering cells consist of a single layer of tall cuboidal or columnar epithelium, the cytoplasm of which is abundant and eosinophilic. The nuclei are round or oval and are central or basilar in position. When the papillae are numerous and cut at right angles to their long axis they give an adenomatous appearance. Usually it is impossible to state from the histologic structure whether an adenoma has or has not produced toxic symptoms. In general, however, lesions which disclose little or no colloid and which are composed of acini lined with tall

The adenomas proper are as variform microscopically as they are grossly, and, accordingly, they may be divided into the following four distinct categories: embryonal, fetal, colloid and papillary. *Embryonal adenoma* (sometimes referred to as undifferentiated fetal adenoma) is the least common. It consists of solid nests or columns of epithelial cells with little or no attempt at forming acini. The cells are rather small and ill-defined; the cytoplasm is moderate in amount and eosinophilic, and the nuclei are round, evenly and lightly stained, and centrally placed (Fig. 173). The supporting stroma consists of well-vascularized, scanty, loose connective tissue.

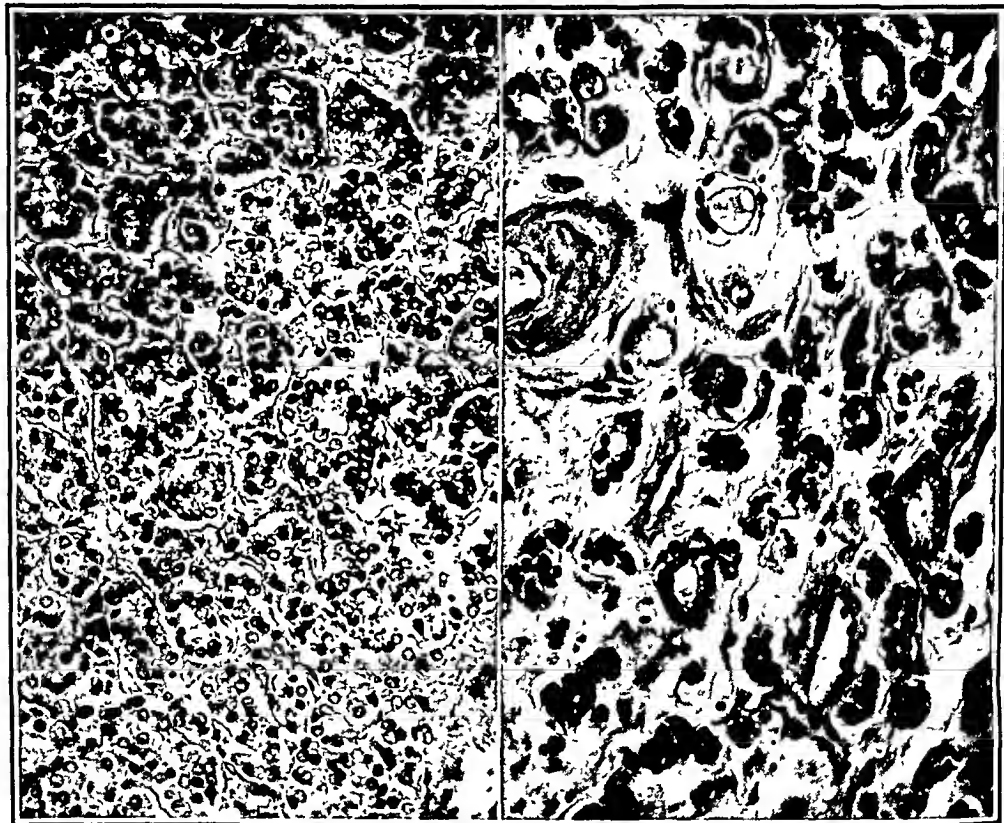


FIG 173.

FIG. 174.

FIG. 173.—Embryonal adenoma. The cells are arranged in solid nests with little attempt at forming acini. x 100.

FIG 174.—Fetal adenoma illustrating small acini and a stroma of hyaline tissue. x 100.

Fetal adenoma has also been called microfollicular adenoma. It consists of numerous small acini lined with a single layer of cuboidal cells (Fig. 174). The cytoplasm is abundant, eosinophilic and laterally not sharply demarcated from the neighboring cells. The nuclei are round evenly stained and centrally placed. The lumens are small and empty or contain scanty colloid. The amount of inter acinar tissue varies. Sometimes it is relatively sparse and rather loose, while at other times it forms broad anastomosing cords or diffuse sheets of densely eosinophilic, homogeneous, acellular material that appears not unlike ordinary colloid. *Colloid adenoma*

of the capsule and invasion of any tissue that it contacts. In the laboratory one encounters tumors of all sizes varying from a small area a few millimeters in diameter to one measuring 10, 12 or more centimeters across (Fig 177). The neoplasm that is grossly detectable is light brown, grey, white or somewhat yellowish. It is usually firm, or hard and solid, or it may contain large areas of necrosis. It involves any lobe, any portion of any lobe or all lobes. It usually starts as a single focus and the uninvolved areas appear as normal thyroid tissue which may or may not contain adenomas. *Histologically*, carcinoma of the thyroid is so pleomorphic and combinations of different cell types are so common that no microscopic classifica-

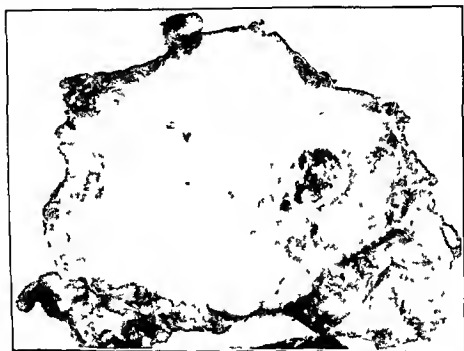


FIG 177 —Advanced carcinoma of the thyroid gland

tion is entirely satisfactory. According to the predominating cells, however, the following *five groups* are recognizable: papillary, adenomatous, diffuse, giant cell and Hurthle cell.

Papillary carcinoma accounts for about one-third of all cases. It arises in the thyroid proper or in an aberrant thyroid and is of low grade malignancy. Frequently, the histologic structure deviates so slightly from an ordinary papillary adenoma that the only criteria of value in establishing a diagnosis of cancer are infiltration of the capsule and invasion of the blood and lymphatic vessels. The tumor is composed of slender stalks of well-vascularized loose or dense connective tissue covered by one or several layers of cuboidal or columnar cells (Fig 178). Their cytoplasm is densely eosinophilic, reticulated or even vacuolated and their nuclei are round or elongated and evenly but deeply stained. In cross section the papillae impart an adenomatous appearance. Colloid may be

columnar cells are most apt to be associated with symptoms of hyperthyroidism.

The *diagnosis* of adenoma of the thyroid is made from a history of a mass in the anterior portion of the neck of long duration that is connected to and moves with the gland. *Treatment* of every adenoma should consist of surgical excision. The *prognosis* in general is excellent. There is no room for prognostication for even in patients with symptomless adenomas, in whom thyroidectomy is not performed, the following *complications* may develop: (1) *carcinoma*. This may be a bonified cancer that is easily diagnosed histologically, or it may resemble an ordinary adenoma and the only indication that it is malignant is invasion of the capsule or blood vessels or the presence of distant metastases. Statistics with regards to the incidence of adenoma developing into a carcinoma vary but it is probable that about 4 per cent will eventually become cancerous. (2) *Toxicity*. This is estimated to occur in approximately 50 per cent of the cases. In addition to those with outright symptoms of hyperthyroidism, there are patients with subclinical manifestations of toxicity in the form of weakness, nervousness and cardiac decompensation, and (3) *local pressure* upon the trachea, larynx and esophagus producing dyspnea, voice changes and dysphagia.

Carcinoma.—Cancer of the thyroid gland is an insidious disease the cause of which is unknown. It is stated that from 37 to 90 per cent of all cases of carcinoma arise in a pre-existing adenoma, and the duration of the benign lesion averages about seven years. Contrary to expectation, a diffuse hyperplasia of the thyroid, rarely if ever, eventuates in a malignant growth and the few cases in which such an association occurs probably have their origin in a small adenoma. The incidence of cancer of the thyroid varies, but the frequency is decidedly more common in goitrous districts. In Switzerland 10 per cent of all surgically removed goiters are cancers, while in Canada less than 1 per cent and in the United States about 3 per cent are malignant. The disease affects females three times as frequently as it does males and is found at all ages from infancy to the eighth decade. Two-thirds of the cases occur between forty and seventy years with an approximate average of forty-eight years for women and fifty-two years for men. When the disease occurs in infancy or childhood it usually arises in aberrant thyroid tissue. The earliest *symptom* is a sudden but progressive increase in size of a nodule of long standing. Symptoms of thyrotoxicosis are present in from 13 to 34 per cent of cases whereas dyspnea, dysphagia, pain, loss of weight, dysphonia, fixation of the mass and hardness are all late manifestations.

Grossly, the lesion varies according to its duration and its histologic composition. In about one-half of the cases a diagnosis of carcinoma is not even suspected until microscopic sections are studied. In such instances the macroscopic appearance is usually that of an ordinary adenoma—the features of which have already been enumerated. When the lesion is large and recognizable clinically, one of the most outstanding characteristics is its penetration

of the capsule and invasion of any tissue that it contacts. In the laboratory one encounters tumors of all sizes varying from a small area a few millimeters in diameter to one measuring 10, 12 or more centimeters across (Fig 177). The neoplasm that is grossly detectable is light brown, grey, white or somewhat yellowish. It is usually firm, or hard and solid, or it may contain large areas of necrosis. It involves any lobe, any portion of any lobe or all lobes. It usually starts as a single focus and the uninvolved areas appear as normal thyroid tissue which may or may not contain adenomas. *Histologically*, carcinoma of the thyroid is so pleomorphic and combinations of different cell types are so common that no microscopic classifica-



Fig 177 —Advanced carcinoma of the thyroid gland

tion is entirely satisfactory. According to the predominating cells, however, the following *five groups* are recognizable: papillary, adenomatous, diffuse, giant cell and Hurthle cell.

Papillary carcinoma accounts for about one-third of all cases. It arises in the thyroid proper or in an aberrant thyroid and is of low grade malignancy. Frequently, the histologic structure deviates so slightly from an ordinary papillary adenoma that the only criteria of value in establishing a diagnosis of cancer are infiltration of the capsule and invasion of the blood and lymphatic vessels. The tumor is composed of slender stalks of well-vascularized loose or dense connective tissue covered by one or several layers of cuboidal or columnar cells (Fig 178). Their cytoplasm is densely eosinophilic, reticulated or even vacuolated and their nuclei are round or elongated and evenly but deeply stained. In cross section the papillae impart an adenomatous appearance. Colloid may be

scanty although it is usually entirely absent, and the tumor is ordinarily surrounded peripherally by a capsule of dense fibrous tissue.

Adenocarcinoma varies tremendously in its degree of differentiation. At one extreme the tumor resembles normal thyroid tissue and at the other the cells are quite bizarre and disclose only a suggestion of alveolar formation. The former appears so innocuous that many writers, albeit erroneously, have termed the lesion "benign metastasizing goiter." The truth of the matter is that the tumor is really an insidious carcinoma which will kill the patient just as surely as will other cancers of the thyroid, the only difference being



FIG. 178

FIG. 179.

FIG 178 —Papillary carcinoma showing thin stalks of connective tissue covered with several layers of hyperchromatic cells. x 100.

FIG 179 —Adenocarcinoma illustrating both a glandular and a more solid or undifferentiated arrangement x 100

that metastases may not become apparent until years after the primary lesion has been detected. One of our patients died of metastasis to the vertebra fifteen years after removal of a "thyroid adenoma." The diagnosis of cancer in these cases rests entirely upon finding neoplastic cells within blood vessels. In the more undifferentiated tumors in this group there are some areas that are more or less solid and others that form definite alveoli (Fig. 179). The former consist of cords or nests separated by varying amounts of loose or dense and sclerotic fibrous tissue. The epithelial cells are rather small and irregular with dense and eosinophilic cytoplasm, or they are of moderate sizes, polygonal and contain lightly

stained reticulated or even vacuolated cytoplasm. The nuclei are uniform and lightly stained. In other areas there are definite acini lined by a single layer of lightly stained, reticulated or vacuolated columnar cells with round or oval uniform nuclei. The lumens are empty or they contain an eosinophilic secretion.

Diffuse carcinoma grows more rapidly than either of the foregoing. It has a tendency to infiltrate between the normal acini and to cause their dissolution by compression so that ultimately there are diffuse sheets of cancer cells enclosing small islands of distorted but still

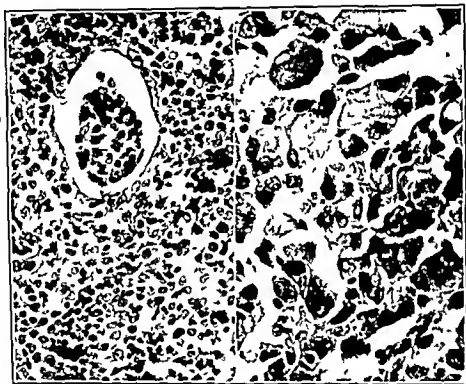


FIG 180

FIG 181

FIG 180 —Diffuse carcinoma composed of small irregular cells with indistinct margins

Note a capillary filled with neoplastic cells $\times 200$

FIG 181 —Giant cell carcinoma showing huge cells with abundant cytoplasm and hyperchromatic single or multiple nuclei $\times 200$

recognizable thyroid tissue. The neoplastic cells are round or irregular but of an overall uniform size of about 12 to 15 microns in diameter (Fig 180). The edges are ill-defined and fuzzy, the cytoplasm is eosinophilic, and the nuclei are round, oval or irregular. Their margins are distinct, they are vesicular or deeply stained, and the chromatin is solid or clumped. Nucleoli are conspicuous. The supporting connective tissue is loose and scanty and the vessels, while not abundant, may be filled with tumor cells.

Giant cell carcinoma is also called *carcinosarcoma*. It occurs in elderly people as a rapidly enlarging nodule that extends widely through the tissues of the neck and penetrates the vessels early.

Histologically, it is composed of collections of huge giant cells embedded in a fibrosarcomatous stroma. The former are composed of variform cells with distinct borders and intensely eosinophilic, abundant cytoplasm (Fig. 181). The nuclei are single or multiple, of many shapes and sizes, hyperchromatic, and dense or reticulated. Nucleoli are usually prominent. The sarcomatous stroma consists of broad intertwining bundles of elongated cells. The borders are indistinct, the cytoplasm is abundant and eosinophilic, and the nuclei are oval, round, elongated or bizarre. Their rims are sharp; their nucleoplasm is washed out; nucleoli are prominent, and mitoses are numerous. The vascularity of these tumors varies and there are usually large areas of complete necrosis.

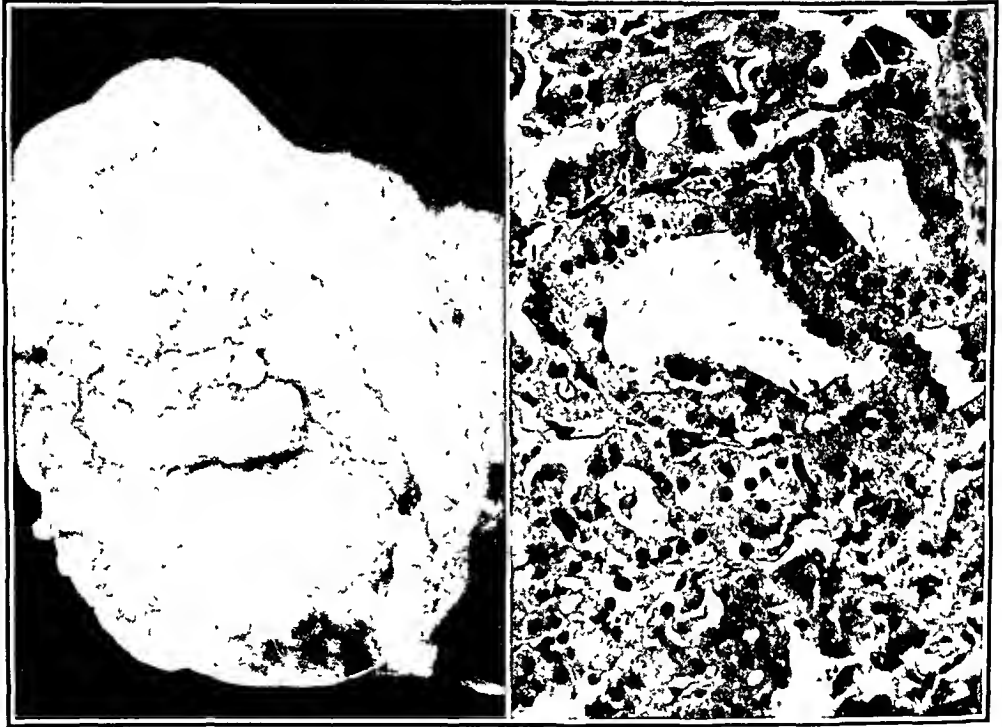


FIG. 182.

FIG 183

FIG 182 —Hurthle cell tumor

FIG. 183 —Same type of tumor. The cells are large cuboidal, intensely eosinophilic and form acini or solid nests x 100.

Hurthle cell tumor is the least frequent and the least malignant. Although some authors divide this tumor into an adenoma and a carcinoma, it is probably safer to regard all of them as low grade carcinomas. The *Hurthle cell* is not a specific normal cell, but it is rather a physiopathologic variant of a thyroid cell. It is large, cuboidal or columnar, and has distinct boundaries and abundant intensely eosinophilic or reticulated cytoplasm. The nuclei are relatively small, round and evenly stained. Neoplasms composed of these cells have been termed Barber cell tumor, Langhans' tumor, Getzowa struma, struma post branchiales (on the assumption that it arose from the post branchial or ultimobranchial bodies), Wurchende struma and small alveolar large cell adenocarcinoma of

the thyroid gland. They affect females much more frequently than males and are found throughout life from infancy to old age. *Grossly*, they are well circumscribed, moderately firm nodules that measure 1 to 10 cm in diameter. Cut surfaces are yellowish grey, finely lobulated and may show areas of degeneration (Fig 182). *Histologically*, they form irregular follicles with or without papillary infoldings or they appear in more or less solid sheets or cords. The cells are similar to "normal" Hurthle cells except that they are larger and less regular. They are cuboidal columnar or polyhedral, sharply defined and have abundant densely eosinophilic reticulated or vacuolated cytoplasm (Fig 183). The nuclei are round, small, intensely stained, and frequently eccentric. The lumens may or may not contain homogeneous pink staining material. The supporting stroma is as a rule scanty, loose, well-vascularized and divides the tumor into irregular lobules.

The *diagnosis* of carcinoma of the thyroid should always be a microscopic one for if one waits until the disease is recognizable clinically it is already too late. *Treatment* consists of prophylactic removal of all nodules, of radical surgical resection followed by roentgentherapy when the disease is not too far advanced, and of palliative irradiation alone in hopelessly advanced lesions. The *prognosis* depends upon the time of diagnosis, the histologic structure and the presence or absence of metastases. If the tumor is suspected clinically the five year survival rate is 20 per cent, if it is first detectable at operation the salvage increases to 40 per cent, whereas if it is found only microscopically, 80 per cent of the patients are well at the end of five years. In general those cancers that histologically resemble normal thyroid tissue (along with Hurthle cell tumors) offer a better prognosis than do the more undifferentiated neoplasms. The outlook in the presence of metastases is hopeless except in instances of so-called "benign metastasizing goiters" in which cures have been reported following removal of a secondary growth.

Exogenous Tumors—The infrequency with which the thyroid gland is involved by exogenous neoplasms has been a point for considerable speculation. It has been postulated that this *relative immunity* is due to (1) a rich blood supply and good venous drainage which inhibits lodgement of tumor emboli, (2) chemical factors (unnamed) that hinder growth, (3) high oxygen content in a normal gland which is incompatible with growth of extraneous cells for these ordinarily require low oxygen tension. By the same token it is stated that secondary neoplasms are more numerous in cases of adenoma because the oxygen supply is reduced. (4) Sieve-like action of the lungs which decreases the number of tumor emboli that reach the thyroid gland and (5) the infrequency with which the thyroid is examined thoroughly. It is said that if the gland was carefully examined at autopsy, the incidence of exogenous tumors would be considerably greater than the figures which at present range from 5 to 8 per cent of all malignant neoplasms coming to necropsy. At some time or other virtually every organ of the body has been reported as harboring a primary tumor that has secondarily

involved the thyroid gland. The *most common* are carcinoma of the gastro-intestinal tract, breast, lung and kidney and melanoblastoma. The *route* of invasion is either by the blood stream or by direct extension from organs such as the larynx, the esophagus and metastatic foci in adjacent cervical lymph nodes. Most of the lesions are incidental findings at postmortem, but a few have been mistaken for primary tumors of the thyroid and have been removed surgically. The *gross* and *microscopic* characteristics, of course, vary with those of the primary neoplasm. The *prognosis* is hopeless.

Mechanical Disturbances.—Mechanical disturbances of the thyroid gland can be reduced to those *consequent to thyroidectomy*. The less serious of these consist of hematoma, collection of serum, brawny edema, tracheal irritation, and foreign bodies as sponges, needles, etc. The more serious and fortunately less and less common are hemorrhage, infection, thyroid crisis, parathyroid tetany, hyperthyroidism and hypothyroidism, and paralysis of the vocal cords. Hemorrhage and infection are rare; thyroid crisis has already been mentioned in connection with diffuse hyperplasia, and parathyroid tetany is considered in the latter part of this chapter.

Hyperthyroidism persisting postoperatively merely means that enough of the gland has not been removed. Unfortunately, there is no accurate way of determining the amount of thyroid tissue to be left intact in any given case, necessitating a complete reliance on the judgment of the operator. Removal of too little tissue results in persistence or return of toxic symptoms for which one or more subsequent operations become necessary. If, on the other hand, not enough functioning tissue remains to take care of the normal body needs, the patient will develop *postoperative myxedema* or as it is often called *cachexia strumapriiva*. Factors responsible for this are: (1) underlying pathologic process as for example thyroiditis when more tissue must be left behind than in diffuse hyperplasia for its function is already impaired, (2) over-suturing of the remaining tissue reducing its physiologic capacity, and (3) prolonged drainage or infection destroying a portion or all of the residual gland. Some or all of the symptoms listed under myxedema in the opening paragraphs of the chapter may develop. They may appear immediately after operation or they may not become apparent until weeks, months or even years later. Sometimes they are transient and are corrected by withdrawing the iodine therapy or by the administration of thyroxin, while at other times they are permanent and necessitate the continuous substitution of thyroid extract.

Paralysis of the vocal cords results from *severance* of the recurrent laryngeal nerves. Its incidence should not exceed 0.3 per cent of all cases of thyroidectomy, and it can be prevented if the nerves are always dissected out and exposed to view before removing any thyroid tissue. The most common position of the recurrent laryngeal nerve is beneath the inferior thyroid artery, but occasionally it may pass over and around this vessel, it may pass directly from the vagus to the larynx or it may divide into its abductor or adductor components before it enters the larynx. *Initially*, a paralyzed vocal cord is lax and can neither be adducted nor abducted but

as it becomes replaced with fibrous tissue, it becomes shorter and fixed in the midline. Unilateral involvement results in no greater interference than cracking of the voice and a decrease in range because the remaining cord compensates. An audible stridor is produced only when there is a greater than normal demand for oxygen such as occurs with excessive emotional or physical activity. Bilateral paralysis of the vocal cords eventuates in immediate loss of voice but no obstruction to breathing. In three to five months as a result of fibrosis and contraction, the cords begin to approximate and first bring about a return of the voice and then gradually increasing dyspnea. The latter is particularly noticeable on exertion, is accompanied by a crowing sound, results in gradual limitation of effort, and can be corrected only by operation upon the cords.

PARATHYROID GLANDS

EMBRYOLOGY

The parathyroid glands first become apparent in the 10 mm embryo as thickenings of the third and fourth pharyngeal pouches. Shortly thereafter they become detached from the pharynx, but the parathyroid arising from the third pouch remains attached to the thymic body and that from the fourth pouch with the ultimobranchial body until the 20 mm stage. With descent of the thymus the former is drawn inferiorly to rest along the inferior border of the thyroid while the latter remains in its original position along the superior border. Cellular differentiation in the primordial glands occurs almost from the start.

ANATOMY

Normally there are four parathyroid glands located along the posterior borders of the lateral lobes of the thyroid gland. The two superior glands are constant in position being found at the level of the lower border of the cricoid cartilage or at the junction of the pharynx with the esophagus. The inferior glands are found at the lower edge of the lateral lobe, some distance below the thyroid or in relation with the inferior thyroid veins. Each gland is dark reddish brown or light tan and is embedded in fat. Its dimensions are 4 to 6 \times 2 to 4 \times 0.5 to 2 mm and its weight is about 0.035 gm. The blood supply comes from the inferior thyroid artery or from an anastomosis between the superior and inferior thyroid vessels, the lymphatics are associated with those of the thyroid, and the innervation comes directly from the middle or inferior cervical sympathetic ganglia or from a plexus on the fascia covering the posterior surface of the thyroid gland.

Histologically, the normal parathyroid gland is composed of a fundamental cell—the chief or principal cell from which probably develop two others—the water clear cells and the oxyphile cells. The proportions of these cells vary with the age of the patient.

Till puberty the entire gland is composed of *chief cells*. These are polygonal, ill-defined cells measuring 6 to 8 microns in diameter. They have scanty, faintly acidophilic, glycogen containing cytoplasm that is retracted from the nucleus, and a relatively large round sharp pycnotic appearing nucleus. Fat does not appear within these cells until after puberty. *Water clear cells* are found occasionally in normal glands after puberty. They measure 10 to 15 microns in diameter, have completely vacuolated cytoplasm, and disclose round pycnotic somewhat eccentric nuclei. *Oxyphile cells* are found in increasing number with advancing age making their first appearance after puberty. They are of two types—pale and dark. At about the age of forty years the former are found in large circumscribed islands. They are polygonal, have sharp borders and dark pink finely granular cytoplasm, and measure 11 to 14 microns in diameter. The nucleus is round and deeply stained. They contain fat but no glycogen. Dark oxyphilic cells are found singly and near the stroma. Their borders are indistinct; they measure 8 to 10 microns in diameter; the nucleus is pycnotic, and the cytoplasm is homogeneously dark red. It contains neither fat nor glycogen. The stroma of parathyroid glands is scanty, loose, well-vascularized and contains an increasing amount of fat until forty years of age. After puberty normal glands frequently contain cysts of varying sizes which are filled with granular and cellular débris or colloid-like substance.

PATHOLOGY

Congenital Anomalies.—The *number* of parathyroid glands is not always constant. There are less than four glands in less than 1 per cent of cases and more than four glands in about one-quarter of all cases. Occasionally some of the glands may be *embedded within the thyroid*; the thyroid or thymus may contain *aberrant* parathyroids, and less often *accessory* glands may be distributed in the soft tissues between their normal positions and the thymus.

Tumors.—Tumefactions of the parathyroid gland are divided into a smaller group—hyperplasia, and a larger group—adenoma. Both are attended by profound and clinically indistinguishable systemic disturbances. The lesions are most common between the ages of forty and sixty years with reported extremes of thirteen and eighty-nine years, and they affect males three times as frequently as they do females. The accompanying *signs* and *symptoms* are protean and may be divided into (1) those due to *hypercalcemia*. Serum calcium in hyperparathyroidism is above the upper limit of normal, namely, 11 mg. per cent and may reach as high as 18 mg. while serum phosphorous is correspondingly decreased below 3.5 mg. per cent. Physiologically, calcium tends to reduce muscular irritability and so in excessive amounts there are: hypotonia, lassitude, weakness, and constipation accompanying which there are also anorexia and loss of weight. (2) Those due to *skeletal involvement*. The source of the hypercalcemia is the bones and depending upon the severity of the disease demonstrable osseous changes or practically the bone may be absorbed. Accordingly,

there may be spontaneous fracture, bony tenderness, pain, deformity, loss of stature, complete inability to walk or even raise the thorax and, radiographically, decreased densities of the bones, cysts and tumors and (3) those due to *renal involvement*. In hyperparathyroidism there is an excessive excretion of both phosphorus and calcium in the urine. These elements may form frank renal calculi or they may precipitate in the renal parenchyma especially the collecting tubules. Consequently, they may be attended by renal colic or impairment of function. Concomitantly, there are polydipsia, polyuria and enuresis.

Grossly, the only finding that helps to distinguish hyperplasia from adenoma is that in the former all glands are usually uniformly enlarged, while in the latter one gland or only a part of one gland is increased in size. The size of the involved gland varies from twice normal to one weighing 300 gm. or to one as large as a "child's head". In general, adenomas are larger than hyperplasias. The gland is encapsulated, smooth, moderately firm or rather soft, cuts easily and presents a deep red, brown



FIG 184—Adenoma of a parathyroid gland

or yellowish grey, homogeneous or partly necrotic and hemorrhagic surface (Fig 184). *Histologically*, a *hyperplastic* gland discloses a monotonously uniform replacement of the normal structure with giant sized water clear cells. They are polygonal, sharply demarcated, measure from 10 to 40 microns in diameter, have clear cytoplasm except for a sprinkling of light pink staining granules, and they contain single or multiple dark round or oval nuclei in which eccentric nucleoli can be frequently discerned. The cells are arranged in alveoli and the nuclei tend to be basilar in position. The connective tissue stroma is uniformly increased in amount throughout the gland and the blood vessels are also evenly distributed and of an unvarying size. In adenoma, if the gland is examined carefully, one will find varying amounts of normal parathyroid tissue around the periphery. Unlike in hyperplasia, *adenoma* presents a mixture of chief, water clear and oxyphilic cells together with transitions between these clear cut and recognizable forms (Fig 185). In general the cells differ from the normal in that they vary in size, show gigantism of their nuclei and reveal extreme hyperchromatism. They form pseudoglands, columns or cords. Chief cells vary in size from 5 to 20 microns. They are distinct or indistinct, have light pink granular or reticular cytoplasm forming a halo around the nucleus and relatively large single or multiple round sharp intensely hyperchromatic nuclei. Water clear cells are similar to those in hyperplasia, but they are less regular whereas oxyphil cells are of normal size, have eosinophilic granular cytoplasm, and a dark irregular nucleus that occupies from one-fifth to three-quarters of the cell volume. Also unlike in hyperplasia, adenoma is accompanied by an irregularly proliferated

stroma. In some areas it is loose and scanty, whereas in others it is abundant and collagenous. Frequently, it contains spaces that are empty or filled with pink material, erythrocytes or desquamated parathyroid cells.

Hyperparathyroidism can be *suspected* only if its protean manifestations are borne in mind. Pertinent signs and symptoms coupled with an elevated serum calcium and a lowered serum phosphorus makes a clinical diagnosis unequivocal. *Treatment* consists of extirpation of the adenoma or one or more hyperplastic glands. Locating the diseased glands, however, is not always easy for they may not be found in their normal positions and when only moderately enlarged they are easily confused with lymph nodes. If the disorder is recognized early the *prognosis* is good but if there is

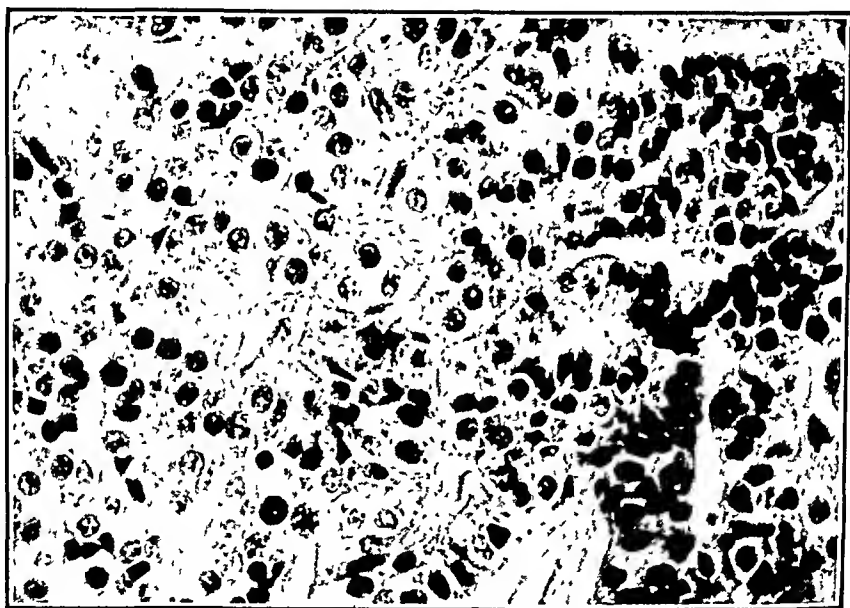


FIG. 185.—Adenoma of a parathyroid gland showing both chief and oxyphil cells
x 200

extensive skeletal or renal involvement or in cases in which the course is fulminating—so-called acute hyperparathyroidism—the prognosis is poor.

Mechanical Disturbances.—The only mechanical disturbance of interest here is that which one way or another destroys the parathyroid glands and results in tetany. *Tetany* after operation may be transient and due probably to edema (for it disappears as the edema subsides) or it may be permanent. The latter is *due to* removal of the parathyroid glands during thyroidectomy, to interference of their blood supply by ligation or by thrombosis, or to subsequent fibrosis. The incidence varies from 0.5 to 1.5 per cent of all operations upon the thyroid gland. It is increased in second and subsequent operations, and is decreased if the following three rules are observed: (1) preserve the posterior thyroid capsule, (2) perform subtotal thyroidectomies, and (3) know the normal and abnormal locations of parathyroid glands. *Signs and symptoms* are

due to a lack of calcium in the blood. When serum calcium is between 4 and 6 mg per cent there are numbness and tingling of the hands, feet, legs and face, carpopedal spasm, violent contractions of the muscles of the face and abdomen initiated by ordinarily inconsequential stimuli, and epileptiform convulsions. When the serum calcium level is between 7 and 8 mg per cent signs and symptoms may not become manifest unless there is excitement, physical exertion, or overbreathing. In tetany of long duration there may develop cataracts, brittle hair, ridged nails and teeth, and disturbances in the gastro-intestinal tract in the form of pains, gas, diarrhea and constipation. *Treatment* consists of administration of parathyroid hormone under which circumstances normal life can be maintained indefinitely.

BRANCHIAL REMNANTS

Early in embryonic life there arises a series of five paired out-pocketings from the lateral walls of the pharynx known as the *pharyngeal pouches*. At the same time there develops a corresponding number of indentations of the overlying ectoderm called the *branchial grooves*. As the two contact each other they push aside the intervening mesoderm to form a series of arches, and the entoderm and ectoderm fuse to form a solid plate. In man this remains intact but in fishes it breaks down to produce a functioning cleft. The *ultimate disposition* of these structures is as follows: groove I forms the external auditory meatus, pouch I—eustachian tube and tympanum, arch I—maxilla and mandible, pouch II—angle of the tonsil, arch II—styloid process, stapes and lesser cornua hyoid bone, pouch III—thymopharyngeal duct, arch III—posterior portion tongue and body of hyoid bone, and pouches III, IV and V lose all traces of a lumen and form the thymus, parathyroid glands and ultimobranchial bodies. Normally, all traces of the original structures disappear, but occasionally remnants of the first and second pouches and grooves develop abnormally or persist post-natally. From the ectodermal portion of the *first pouch* there may arise *pre-auricular appendages* or *sinuses* which are often associated with malformations of the ear proper. Abnormalities of the *second pouch* and groove consist of a *sinus* if either end is open, of a *fistula* if both ends are open and of a *cyst* if both ends are closed. The latter is three times more frequent than the former two.

Branchial cysts have also been called sequestration dermoids, dermoids, atheromatous tumors and hydrocele colli congenita. They are noted at any time from infancy to old age, affect females almost twice as frequently as males, are usually unilateral, are located below the angle of the jaw anterior to the sternomastoid muscle, and measure 1 to 10 cm in diameter. *Symptoms* in order of frequency consist of painless swelling that may vary in size, swelling associated with an upper respiratory infection, draining sinus, pain, dysphagia, fever and dysphonia. Many of the smaller tumors are cystic to palpation but as they enlarge they become firm and feel more solid. Their external surface, particularly if they

have been previously infected, is adherent to surrounding structures by dense fibrous tissue. They are round or ovoid; their walls are paper thin or measure a centimeter or more in diameter; the inner surface is smooth, granular, polypoid or papillomatous with often fibrous trabeculations, and they are usually filled with thick greasy or flaky grey to brown semisolid material and less often with mucoid, watery or milky fluid (Fig. 186). *Histologically*, the lining in those cysts which arise from branchial grooves (outer portion) is composed of stratified squamous epithelium, while in those which arise from pharyngeal pouches (inner portion) is composed of pseudostratified ciliated columnar epithelium. The former is by far the more frequent. In either case, the epithelium lies directly

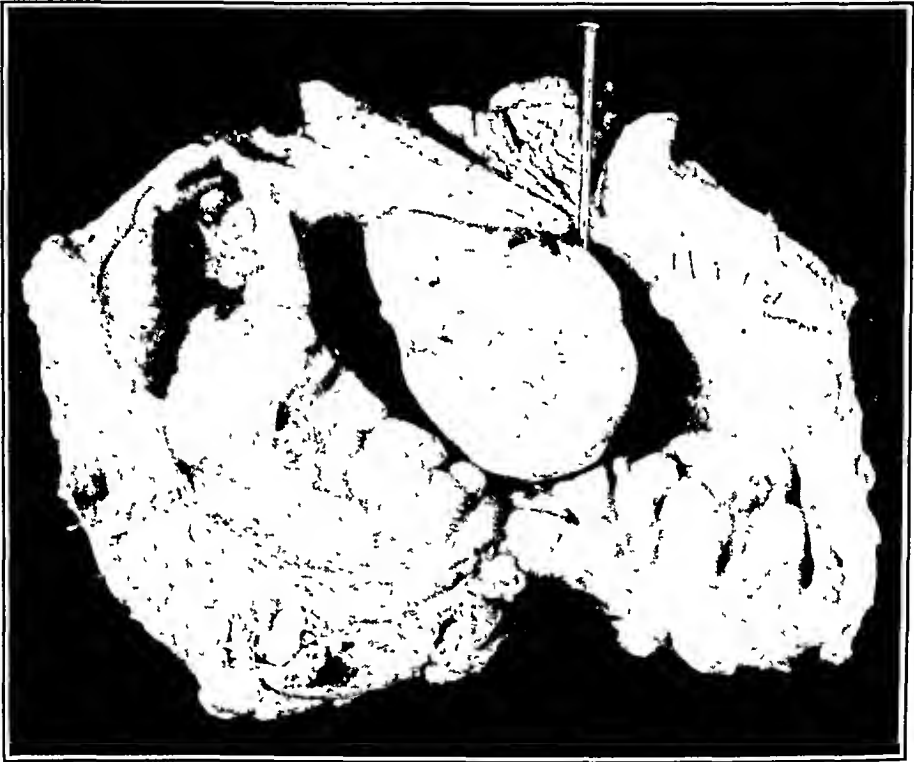


FIG. 186.—Branchial cyst The pin rests in the external opening The polypoid masses are composed of lymphoid tissue

upon a band of lymphoid tissue, either diffusely arranged or forming discrete follicles with conspicuous germinal centers. Beyond this, there is a layer of connective tissue. Infected cysts show partial or complete denudation of the epithelium, infiltration of the wall with leukocytes and varying degrees of fibrosis. *Treatment* consists of conservative measures in acutely inflamed cysts followed by incision and drainage if the process does not resolve. Complete excision is indicated after the infection has subsided or in non-infected cysts. The *prognosis* is good.

Branchial carcinomas are comparatively rare. It is always hazardous to make a diagnosis of cancer arising in a branchial rest, because one can never be absolutely certain that the lesion in question is not a metastasis from some undiscovered focus elsewhere

in the body. This is especially true of the solid growths. The criteria for accepting such a diagnosis must, therefore, be rigid. The tumor must be in the right location, that is, in the lateral side of the neck below the angle of the jaw, it must be partly cystic, the wall must be lined with stratified squamous or pseudostratified columnar epithelium resting upon a band of lymphoid tissue, the infiltrating tumor must arise from the lining epithelium, and there must be no other demonstrable primary foci elsewhere in the body. Cancer of branchial remnants affects men more frequently than women, is usually seen after forty years of age, involves each side with equal frequency, is rarely bilateral, and is rapidly growing. Symptoms consist of a tumor which is associated with local or radiating pain, and examination reveals a firm cystic or hard mass that is attached to the surrounding structures. Grossly, the neoplasm is usually 3 to 4 cm in diameter, is composed of a cystic portion similar to a branchial cyst already described, and it has attached to the cyst a solid mass of tissue. This varies in size, is usually firm, and on cut surface is tan, grey or white with scattered yellow necrotic foci. Histologically, the wall of the cyst is typically that of a branchial cyst and is, therefore, ordinarily lined with stratified squamous epithelium. The latter penetrates the underlying tissue in the form of irregular nests or strands of epithelial cells that present the usual characteristics of squamous cell carcinoma. The supporting tissue is either lymphomatous or it is dense acellular and fibrous. Treatment consists of surgical excision followed by irradiation. The prognosis is poor. Most of the patients die within a few months.

CAROTID BODY TUMOR

The carotid body has also been called glomus caroticum, carotid gland and paraganglion intercaroticum. It is a small mass of well encapsulated or reddish brown tissue measuring 2 to 5 mm in diameter that is situated postero-medial to the distal end of the common carotid artery. Histologically, it is composed of large masses of polygonal chromaffin cells exhibiting distinct borders, granular or foamy cytoplasm and round basophilic centrally placed nuclei. The stroma of connective tissue arises from the capsule, the nerves come from the plexus around the carotid artery, and the blood supply is derived from the external carotid artery. The origin of the carotid body is not agreed upon. It is said to arise from the same tissue that gives origin to the superior cervical sympathetic ganglion, from the adventitia of the external carotid artery and from the third branchial pouch. Although it resembles the adrenal medulla, aortic body, hypophysis, coccygeal body and paravertebral sympathetic ganglia, its function is not clear. Because of its proximity to the carotid sinus, the function of the latter has been interpreted as that of the carotid body. When the carotid sinus is compressed the pulse shows and the blood pressure falls, and when pressure is released or decreased the opposite is true.

The only significant lesion of the carotid body is the carotid body tumor. Although this lesion has also been called perithelioma,

perivascular endothelioma, alveolar tumor, chromaffinoma, pheochromocytoma and paraganglioma such designations do nothing more than confuse the reader. The neoplasm is not rare there having been at least 275 cases recorded in the literature. It is as a rule unilateral, affects both sexes with equal frequency, has a tendency to be familial and is usually found between the ages of twenty to sixty years. The chief *symptom* is a slowly enlarging mass in the side of the neck that is usually present for a half a dozen years before medical aid is sought. Attacks of syncope with lowering of blood pressure in a few patients are attributable to pressure

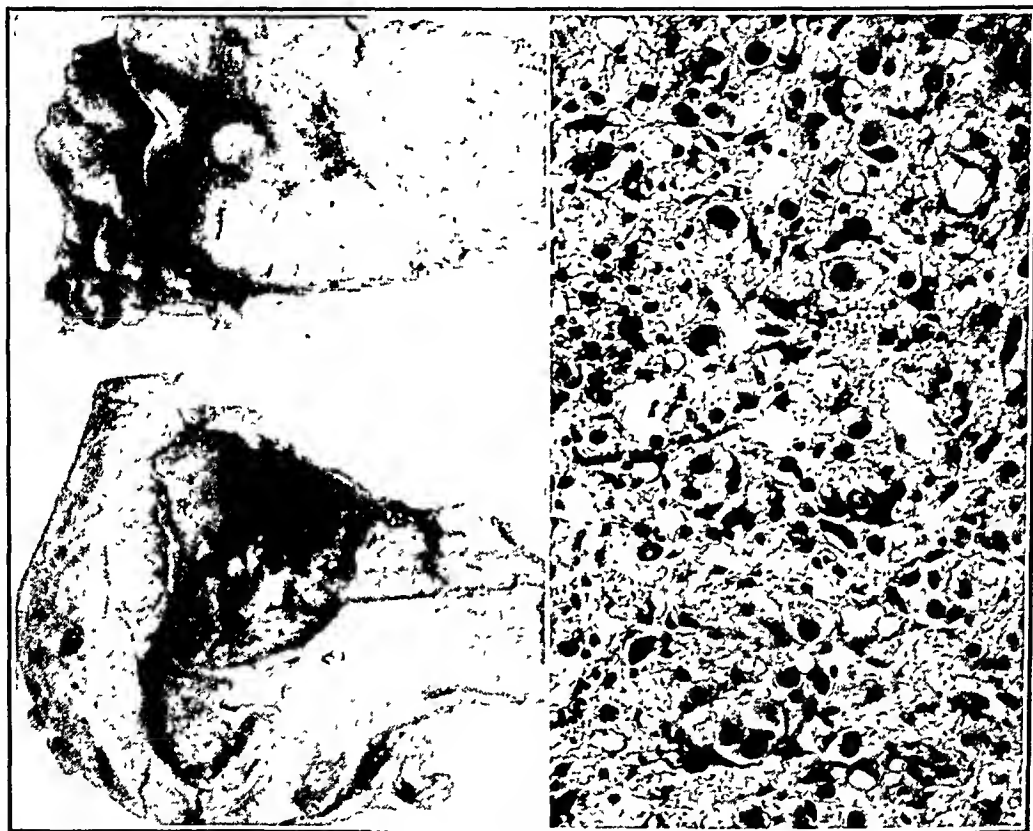


FIG. 187:

FIG 188.

FIG 187.—Carotid body tumor showing both external and cut surfaces. Attached to the capsule is a portion of the common carotid artery.

FIG 188.—Carotid body tumor composed of reticulated and vacuolated polyhedral cells. x 100.

upon the carotid sinus rather than to secretions or stimuli from the tumor. Less commonly there may be hoarseness, dyspnea, dysphagea and Horner's syndrome—all due to involvement of pertinent nerves. The mass is firm or soft and moves freely laterally but not up and down.

Grossly, the tumor is well encapsulated, measures as much as 9 cm. in diameter but is ordinarily one-half this size, and either bears the imprints of the carotid vessels upon its surface or has these arteries attached to its capsule or embedded within its substance (Fig. 187). Cut surfaces are composed of solid greyish, brownish or yellowish tissue traversed by hemorrhagic fibrous tissue septa.

In larger tumors there may be foci of degeneration or cyst formation filled with bloody material. *Histologically*, large, polyhedral, well-defined, granular foamy or vacuolated cells are arranged in solid alveoli, groups or cords (Fig 188). The nuclei are usually single, round, oval, deeply basophilic, relatively small and central or slightly eccentric in position. Sometimes, however, they are multiple, large, and intensely hyperchromatic. The stroma is scanty, loose or dense, cellular or hyaline, and as a rule vascular. Thin walled capillaries are also numerous between the tumor cells.

A preoperative *diagnosis* of carotid body tumor is not usually made. It should be suspected in the presence of any slowly progressive swelling in the region of the bifurcation of the common carotid artery that starts around puberty and that is movable laterally not superiorly and inferiorly. Attacks of syncope and low blood pressure facilitate a correct diagnosis. *Treatment* consists of complete surgical excision. This can be accomplished with impunity when the lesion is small, but is hazardous when it is large for then the tumor encases the carotid vessels and nerves in the vicinity. When ligation of the internal carotid artery is necessary, the operative mortality is 30 per cent. In such cases the chief complication is hemiplegia. If vessels and nerves are not involved the *prognosis* is good. A *malignant transformation* is extremely rare.

LYMPH NODES

The subject of lymph node enlargements is considered in greater detail in Chapter XVI (p 484). In the cervical region diseases of lymph nodes account for the majority of tumefactions. The only important *congenital* lesion is a *lymphangioma* which presents all the characteristics already enumerated in Chapter 1. *Inflammatory* lesions consist of *acute or chronic non-specific infections* that arise from abrasions, ulcerations or abscesses within the mouth, nasopharynx, upper part of the esophagus or the larynx. It should be noted that an ulcerating carcinoma in these same areas will often be accompanied by a simple non-specific inflammation of the draining lymph nodes, and that such enlargements are, therefore, not always due to neoplastic metastasis. Of specific inflammations, *actinomycosis* is rare, *syphilis* in both the secondary and the tertiary stages is more common, and *tuberculosis* is quite frequent. The latter is often referred to as *scrofula*. It is most common among children of poor communities and, particularly, among those of the negro race. The organism, either the bovine or the human tubercle bacillus, gains entrance through abrasions of the mucosa of the mouth, nasopharynx and especially the tonsils. The site of inoculation, however, is usually free of tuberculosis. The draining lymph nodes are large, matted, soft, caseating and characteristically perforate the skin to produce sinus tracts. *Histologically*, they may disclose tubercles or merely tuberculous granulation tissue. *Tumors* of cervical lymph nodes are the most common causes of enlargement. Primary lesions consist of the entire group of *lymphoblastomas* which is considered in Chapter XVI. Of particular importance are

metastatic carcinomas from the nasopharynx, for the primary tumor is often only a few millimeters in diameter, while the metastases in the neck measure a dozen centimeters or more across. We repeatedly see such patients referred to the tumor clinic who for months have been regarded as harboring a primary lymphoblastoma simply because no one took the trouble of examining the nasopharynx. *Mechanical disturbances* are those concerned with pressure of any enlarged lymph nodes upon the trachea, esophagus, blood vessels and nerves resulting respectively in dyspnea, dysphagia, edema and nerve root pain. When the latter involves the brachial plexus and the inferior portion of the cervical sympathetic chain it produces the typical Pancoast syndrome.

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CHAPTER VII

MEDIASTINUM

THYMUS

EMBRYOLOGY

THE thymus first appears in the sixth week of embryonic life as an outpocketing of each *third pharyngeal pouch*. The analges are first hollow but soon become solid bars. By the eighth week the lower portions contact each other and soon thereafter they descend into the thorax, while the upper portions attenuate and then disappear. By the tenth week the original epithelium is transformed into reticular tissue and thymic corpuscles (Hassall's). By the third month lymphoid tissue becomes prominent, the organ differentiates into a cortex and a medulla, and its development is completed.

ANATOMY

The *normal thymus* is essentially a flat paired organ composed of two lobes that are loosely united by connective tissue and rarely separated by a third lobe. It is located in the superior and anterior portion of the mediastinum lying beneath the sternum, covering the upper portion of the pericardium and the great vessels, and extending from the base of the neck to the level of the fourth costal cartilage. It is encased in a connective tissue capsule which sends septa into the gland to form lobules that measure 0.5 to 2 mm. in diameter. The size of the gland is not static. At birth it weighs about 13 gm., by puberty 35 gm. and by the sixtieth year 10 gm. Normal involution is greatly enhanced by cachexia and infection.

Histologically, the gland is divided into an outer portion—the *cortex* and an inner portion—the *medulla*. Its three most important components are thymocytes, reticular cells, and thymic (Hassall's) corpuscles (Fig. 189). *Thymocytes* are predominantly in the cortex. They are small, round cells with scanty or imperceptible cytoplasm and uniform evenly stained nuclei. While some authors maintain that they arise from thymic epithelium most writers believe they are mesenchymal in origin and that they are in reality lymphocytes. The occasional presence of true lymphoid follicles strengthens this contention. *Reticulum cells* are found both in the cortex and the medulla, but are more prominent in the latter. They are of two types—one derived from the original epithelium and one, albeit in minority, from mesoderm. This distinction, however, is not apparent histologically for each is composed of elongated, peripherally indistinct cells with a moderate amount of pale eosinophilic cytoplasm and round or oval lightly stained nuclei. *Thymic corpuscles* are round structures measuring 30 to 100 microns in

diameter and composed of concentrically arranged, eosinophilic cells. Their centers may undergo degeneration, hyalinization, cystic formation or calcification. They are derived from epithelium and are found in the medulla. Aside from these cells the thymus contains a few eosinophiles and plasma cells.

Other than forming lymphocytes, myelocytes and plasma cells the functions of the thymus gland are not well understood. While experimental data on its hormonal tie-up is contradictory there are indications (1) that involution is produced by hypophysectomy, gonadotropins, sex hormones, cortin and adreno-cortico-tropic

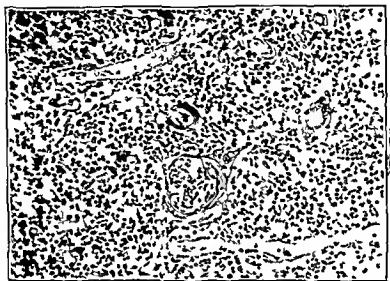


FIG. 189.—Normal thymus showing thymic corpuscles, thymocytes and reticular cells. $\times 100$

hormones, (2) that gonadectomy in young animals delays involution and (3) that administration of the growth promoting hormone of the anterior pituitary causes enlargement.

PATHOLOGY

Congenital Anomalies—Developmental abnormalities of the thymus are of little clinical significance. There have been described (1) *hypoplasia* of either one or both lobes, (2) *aberrant* thymic tissue. This may occur in either side of the neck at any point between the pharynx and the normal position of the gland and it may be associated with a normal, hypoplastic or aplastic corresponding lobe of the thymus. Sometimes pieces of thymic tissue are found in the thyroid gland or surrounding the parathyroids. (3) *Persistent thymo-pharyngeal ducts*, (4) *cysts* derived from these ducts and (5) *inclusions* within the thymus of thyroid and parathyroid tissue.

Inflammation—*Acute inflammation* of the thymus may be found as a terminal event in any debilitating disease in which case the

organ is enlarged, boggy and soft. Histologically, there is considerable edema and a diffuse infiltration with neutrophils, eosinophils and plasma cells. Sometimes, in pyemia or as an extension from an adjacent organ, there may be present *acute abscesses*. These, however, are usually incidental findings at autopsy. *Specific inflammations* are likewise of little surgical importance. *Tuberculosis* of the thymus is sometimes encountered as part of a systemic miliary infection whereas *syphilitic* involvement is almost confined to the congenital form of the disease. The process is usually diffuse and is accompanied by considerable fibrosis. Gummas, although described, are rare. Occasionally, in newborn infants, there are found small miliary or conglomerate abscesses that supposedly originate as central necrosis of thymic corpuscles. These are referred to as *Dubois abscesses*. They are generally considered as syphilitic in origin, and while, ordinarily, they are of little significance, they may become large enough to produce compression of the trachea and asphyxia.

Tumors.—Tumefactions of the thymus may be divided into two categories—benign consisting of a hyperplastic or persistent thymus and malignant which may be conveniently considered under the one heading—malignant thymoma.

Hyperplastic or Persistent Thymus. These are terms used to indicate an enlargement of, or an abnormal involution of, a thymus in a patient of that particular age group. Sometimes this is extremely difficult to establish with any degree of certainty for the thymus is not a stable organ and, although its normal weights as listed in the beginning of this chapter are averages, they vary considerably from case to case within a given age group. In addition, as already stated, the nutrition and general health of the patient has a direct bearing on the size and weight of the organ. Nevertheless, despite these discrepancies it is well established that the thymus is frequently *enlarged* or *persistent* in the *following diseases*; exophthalmic goiter, Addison's disease, acromegaly, rickets, status thymico-lymphaticus, and myasthenia graves. Since only the latter two directly concern the surgeon they alone will be considered further.

Status thymico-lymphaticus may be defined as an enlargement of the thymus and lymph nodes and a hypoplasia of the heart, aorta and both the cortex and medulla of the adrenal glands. Its single pertinent *clinical* manifestation is sudden death that results from even trivial injuries. It is in this respect that the syndrome is of importance to the surgeon for these patients frequently die from the prick of a needle or a whiff of anesthetic far below the lethal or even the proper anesthetic dose. The exact *mechanism* eventuating in *death* has not been agreed upon although it is probable that in a given case any one of the following four factors may be responsible: (1) *mechanical pressure* of the thymus upon the trachea, great vessels and nerves, (2) liberation of a *thymic toxin*, for it has been shown that injections of a thymic extract produce shock in experimental animals, (3) *anaphylactic* reaction due to escape of nucleoproteins from necrosis of germinal centers of the lymph

nodes and (4) an *adrenal insufficiency*. It must be admitted, however, that although the acceptance of this syndrome is justified



FIG 190 —Myasthenia gravis, disclosing foci of lymphocytic cells between muscle fibers $\times 200$

in a select group of cases the entity has fallen into disrepute because the diagnosis is only too frequently used as a cover-all

Myasthenia gravis is an uncommon disease of the *myoneural junction* characterized by easy fatigability of the voluntary muscles. Normally acetylcholine is necessary at the synapse for proper conduction of nervous stimuli. Continued transmission of these impulses is prevented by an enzyme—cholinesterase which splits acetylcholine and, thereby, inhibits its conducting capacity. In myasthenia gravis there is a relative overactivity of the enzyme. The disease is of a few months or many years duration, affects females four times as frequently as it does males, and is usually manifest between the ages of fourteen and fifty years. Some of the more common symptoms are diplopia, dysphagia, nasal speech, ptosis, dyspnea, weakness of the muscles of the jaw, neck and extremities, and loss of facial expression. The only constant pathologic change is in accumulation of lymphocytes at the myoneural junctions known as lymphorrhages (fig 190). In over half of the cases there is in addition a persistence, a hyperplasia, or a tumor of the thymus gland. Pathologically, the non-neoplastic glands show age involution, increase in lymphocytes, loss of differentiation between the cortex and medulla, or an increase in



FIG 191 Thymoma from the same case of myasthenia gravis shown in figure 190. It is cystic and the capsule is calcified. Natural size

germinal centers in the medulla. The neoplastic thymuses, on the other hand, are either solid or cystic, yellowish grey or light brown, may be partly calcified and measure from 4 to 8 cm. in greatest diameter (Fig. 191). *Histologically*, they do not differ from the thymomas which are not associated with myasthenia gravis. The exact relation between the thymus and the disease is not known, but it is known that thymectomy greatly improves or cures patients who have had symptoms less than one year. This, therefore, constitutes one form of *treatment*. It is, however, not advocated in all cases for it has also been well established that prostigmine inactivates cholinesterase and its administration will completely control about 25 per cent of the cases. Indications for operation are (1) the presence of a thymoma and (2) disability despite the use of prostigmine. The *mortality* in untreated cases is about



FIG. 192—Thymoma of the lymphosarcoma variety.

80 per cent; in those treated with prostigmine it is approximately 22 per cent, whereas in patients submitted to thymectomy the operative mortality is 20 per cent.

Malignant Thymoma.—This term was coined as an all inclusive name for the various types of malignant neoplasms of the thymus gland at a time when their histogenesis was in a state of confusion. While today complete agreement as to their origin is still lacking and while a uniform nomenclature still does not exist, the basic pattern has been well enough established to permit an acceptable and useful classification. In general, malignant thymomas occur at all ages from infancy to the sixth decade; they affect males twice as frequently as they do females, and they are not accompanied by any early *signs* and *symptoms*. The latter become manifest only as a result of pressure upon vital structures and as such they may consist of intermittent dyspnea, hoarseness, orthopnea,

cyanosis, cough, dysphagia, and swelling of the chest, neck, face and arms. Physical examination may show a fulness in the supra-sternal notch and dullness on either side of the sternum. Roentgenograms will disclose a shadow beneath the sternum in the anterior mediastinum.

Grossly, the neoplasm is located in the anterior mediastinum in the region of the thymus (Fig 192). When the lesion is small, it often maintains the shape and even the size of the normal gland. As it becomes larger, it becomes more irregular and more lobulated but it retains its encapsulation for a considerable time. It spreads in a sheet-like manner superiorly to the neck, inferiorly over the pericardium and heart to as low as the diaphragm, laterally to involve the pleuras, and posteriorly to infiltrate between and to surround all of the structures in the mediastinum. In advanced cases the under surface of the sternum and ribs may be eroded but as a rule these escape injury. The colors of the tumors vary from light brown to yellowish grey or white, whereas the consistency ranges from soft and brain-like to a hard unyielding scirrhus mass. Usually the neoplasms are solid but occasionally there are foci of necrosis, hemorrhage and even liquefaction with cyst formation. The latter are frequently surrounded by a calcified capsule of fibrous tissue. Histologically, malignant thymomas may be divided into the following four categories, (1) lymphosarcoma, (2) Hodgkin's disease, (3) lymphoepithelioma and (4) carcinoma. *Lymphosarcoma* is the most common and is the usual type of thymic tumor seen in infants, children and young adults. It is composed entirely of small or moderately sized round cells with scanty, almost imperceptible cytoplasm and round evenly stained nuclei. These cells are indistinguishable from lymphocytes and lymphoblasts. In a few recorded cases tumors of this group terminated with a peripheral blood picture of lymphatic leukemia and have, therefore, been called *leucosarcoma*. *Hodgkin's* variety of thymoma is considerably less frequent than the lymphosarcomatous type and most of the recorded cases have been in adults. The microscopic structure is identical with that of Hodgkin's disease elsewhere. The normal architecture is completely replaced with a diffuse and varied increase of fibrous tissue and cellular infiltrate. The latter consists of plasma cells, lymphocytes, neutrophils, monocytes, occasional eosinophils, and typical Sternberg-Reed cells. There may or may not be foci of necrosis and hemorrhage. *Lymphoepitheliomatous* variety of thymoma is the most frequent type found in adults. As the name indicates it is composed of an admixture of both lymphocytes and epithelial cells derived from the entodermal reticulum (Fig 193). The latter consist of ill-defined clusters, cords or sheets of rather large, pale staining, elongated or polygonal cells. Their borders are indistinct and their cytoplasm is lightly eosinophilic and reticulated. Their nuclei are round or oval, sharply defined, lightly stained, and sometimes contain nucleoli. There are few or no mitoses. The proportion of lymphocytic cells to reticulum cells varies from case to case and even in different areas of the same tumor. When one type equals the other the

resulting picture is that of lymphoepithelioma, but when lymphocytic cells predominate it becomes a lymphosarcoma, and when reticulum cells predominate it becomes a carcinoma. In some cases the reticulum cells have a tendency to be disposed around capillaries in a characteristic manner. Those nearest the vascular wall become slightly elongated and are arranged at right angles to the vessel (Fig. 194). They do, however, appear similar to and are intimately connected with the more distant cells. Tumors presenting this arrangement have been called peritheliomas under the assumption that they arise from "perithelial cells"—whatever they may be.

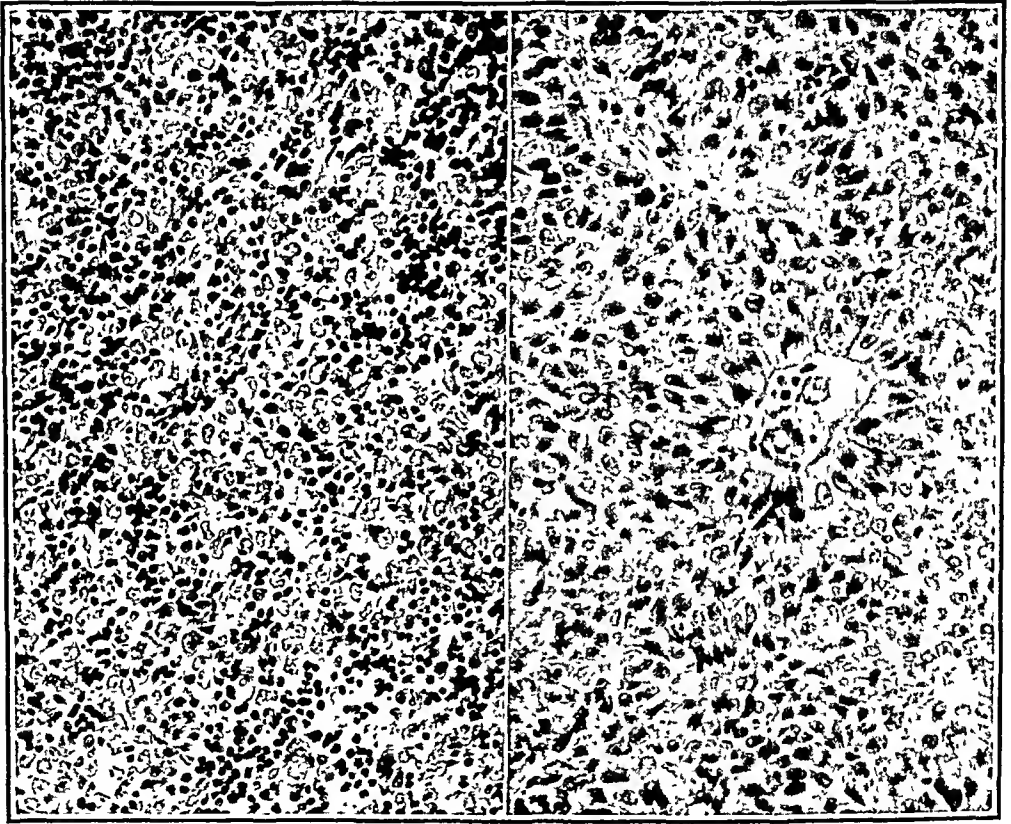


FIG 193.

FIG 194

FIG 193 —Lymphoepithelioma of the thymus. The lymphoid cells are small round and dark. The epitheliomatous cells are large ill-defined and lightly stained. $\times 100$.
 FIG. 194 —Thymoma. The reticular cells are disposed about a capillary rendering what has been called a "peritheliomatous" appearance.

My own experience has been that there is, therefore, no room for a separate subdivision. *Carcinoma* of the thymus is the least common and, as already mentioned, it is a one-sided development of the lymphoepithelioma. *Histologically*, therefore, it is composed primarily of diffuse masses of polygonal or elongated reticular cells among which are deposited varying numbers of irregular thymic corpuscles (Fig. 195). These are large or small and are composed of concentrically arranged, light staining, flat or elongated cells with moderate eosinophilic cytoplasm and oval, elongated light staining or pycnotic nuclei. Their centers may be cellular, hyalinized, granular or completely necrotic and their peripheral cells are

continuous with those of the tumor proper. It should be pointed out, however, that thymic corpuscles are also seen in the other varieties of thymoma, albeit in fewer numbers.

As already indicated, malignant thymomas spread by direct and lymphatic extension to involve the mediastinal structures, pleuras and diaphragm in which case they are often associated with effusions. Metastases to the lungs and axillary lymph nodes are not unusual, but distant metastases to the liver, pancreas, adrenals, kidneys and bone, while described, are infrequent.

Except for the cases associated with myasthenia gravis, a diagnosis of thymoma is usually not made until the disease is advanced. The most important single aid in arriving at a correct clinical solution is a roentgen demonstration of a mass in the region of the thymus.

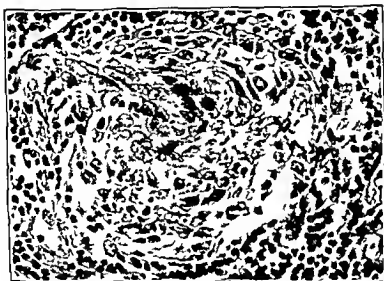


FIG. 19a.—Neoplastic thymic corpuscle. Note the cellularity as compared with a normal corpuscle illustrated in figure 189. $\times 200$

Treatment of the smaller and more circumscribed lesions and particularly those associated with myasthenia gravis is thymectomy, whereas that of the larger tumors is irradiation therapy. The initial response in the lympho-epitheliomatous type and some of the Hodgkin's variety is good, but the tumors rapidly recur. The lympho-epitheliomatous and carcinomatous types on the other hand are radioresistant. The duration of the disease from onset of symptoms to death varies from one to eighteen months.

Mechanical Disturbances—There are no noteworthy mechanical disturbances in the thymus proper. As already stated, however, an enlargement of this organ, particularly when it contains a tumor, produces pressure upon vital mediastinal structures. Compression of the trachea results in dyspnea, obstruction of the veins eventuates in edema of the arms, neck, face, and thoracic wall and effusion into the pleural and pericardial cavities and encroachment upon the esophageal lumen produces dysphagia.

LYMPH NODES

Diseases of mediastinal lymph nodes are of greatest surgical importance from the viewpoint of a differential diagnosis. The lesions encountered are the same as those seen in lymph nodes elsewhere in the body and since these are considered in more detail in Chapter XVI only the more common ones need be mentioned here. *Lymphangioma* is rare. *Tuberculosis* and *Boeck's sarcoid* constitute the important inflammatory disorders while primary neoplastic processes consist of *lymphosarcoma*, *Hodgkin's disease* and *reticulum cell sarcoma*. *Metastatic carcinoma*, especially primary cancer of the lungs, is perhaps as common as are the primary growths. Frequently, these cannot be distinguished, for even radiologically each presents merely a broadening of the mediastinum. In such instances, and particularly when there are no peripheral nodes for biopsy and the bronchoscopic and cytologic examinations of bronchial secretions are negative, one may be forced to resort to a therapeutic test of irradiation. Cancerous nodes will not respond to roentgen treatment, whereas lymphoblastomatous nodes frequently "melt" away even with minute doses. *Mechanical disturbances* of mediastinal lymphoid structures consist (1) of rupture of the thoracic duct which results in chylothorax and (2) of pressure upon the trachea, esophagus and veins eventuating in corresponding symptoms of occlusion.

SOFT TISSUES

Congenital Anomalies.—The only significant, albeit extremely rare, developmental abnormality of the mediastinum is an *opening* in its *anterior portion* resulting in a direct communication between the two pleural cavities. The *genesis* of this defect is readily explained embryologically. As the lung buds push into the spongy mesenchyme laterally, they split off the pericardium from the lateral wall and as the lungs develop further they flank the heart on each side and approach each other anterior to the pericardium. Their covering mesothelium becomes the visceral pleura. Normally the pleuras of each cavity are separated from each other anteriorly by a broad space filled with loose areolar connective tissue containing vessels, nerves and lymphatic tissue. Abnormally an encroachment of the lungs anterior to the heart may decrease the space to a mere septum or may cause complete absorption of even the septum thus producing a free communication between the right and left pleural cavities. In the absence of pulmonary disease patients with such a defect have no referable *symptoms* but if for some reason the intrapleural pressure in one cavity is increased it will directly affect that of the other cavity resulting in pain, cyanosis, and extreme dyspnea. Of the recorded cases, increased pressure has usually resulted from spontaneous or artificial pneumothorax in patients with pulmonary tuberculosis. The *diagnosis* is confirmed fluoroscopically and radiologically. If symptoms persist or recur the *treatment* is surgical closure of the defect otherwise operative interference is not justified.

Inflammation—The only important inflammatory lesion in the mediastinum is *nonspecific acute mediastinitis*. Aerobic and anaerobic organisms, such as *streptococcus hemolyticus* and Vincent's spirochaetes, are the precipitating causes whereas the predisposing factors may be listed as follows: (1) traumatic which include instrumentation of the esophagus and less often the trachea and bronchi, operations on the lung and mediastinum, swallowing of foreign bodies, and external injuries to the chest wall, (2) extension of inflammatory lesions from nearby tissues and organs as mediastinal lymphadenitis, suppurative cervical lesions, empyema, pericarditis, osteomyelitis of sternum, ribs or vertebrae and subphrenic abscess, (3) neoplastic as ulcerating carcinoma of the esophagus and (4) hematogenous metastasis from elsewhere in the body. Of the aforementioned predisposing causes, perforation of the esophagus by swallowed foreign bodies accounts for over 50 per cent of all cases of acute mediastinitis, and the objects most frequently encountered are fish and chicken bones. Clinically significant is a history of sudden pain after eating fish or chicken, or after esophagoscopy or esophageal dilatation. Frequently, the pain is aggravated by swallowing and there may be an accompanying subcutaneous emphysema of the neck. In addition there may be chills, fever, dyspnea, dysphagia, prostration, leukocytosis and rapid pulse. Roentgenograms may show air in the mediastinum, anterior dislocation of the trachea and a wide mediastinal shadow with often a sharp outline.

Pathologically, the lesions are of three types—phlegmonous, gangrenous, and focal suppurative (abscess). *Phlegmonous mediastinitis* is a rapidly spreading diffuse inflammation of the connective tissue. There are edema, an outpouring of leukocytic cells, and a proliferation of connective tissue resulting in induration and matting of all the structures. The tissues in the posterior mediastinum are most severely affected, and in these areas there may form small foci of necrosis with complete liquefaction. *Gangrenous mediastinitis* is the type of infection seen after perforation of the esophagus. It is due to anaerobic organisms derived from the mouth and is characterized by a rapidly spreading greenish grey, foul smelling, liquefaction of all the soft tissues with little or no attempt at localization. *Mediastinal abscess* usually results from a downward extension of an inflammatory lesion in the neck. The infection reaches the mediastinum by following along the fascial planes, the vascular sheaths, or by way of the lymphatics. The process is usually localized in the posterior portion of the upper part of the mediastinum at a level not lower than the bifurcation of the trachea.

A diagnosis of mediastinitis is made from a history of sudden pain in the posterior portion of the chest following esophageal instrumentation or swallowing a foreign body. It is confirmed by demonstrating roentgenographically a broadened mediastinum, air in the mediastinum or an anteriorly displaced trachea. Treatment is not standardized. Some observers advocate immediate surgical drainage either through the neck or posteriorly through the chest.

wall, whereas others recommend watchful waiting, symptomatic measures and chemotherapy. *Complications* that may arise are: pleuritis, pleural effusion, pleural empyema, pulmonary abscess, pericarditis, retroperitoneal abscess and peritonitis. The *prognosis* must always be guarded for the mortality rate is high.

Tumors.—Neoplasms of the thymus have already been discussed and those of lymph nodes have been mentioned. In addition almost all of the remaining tissues in the mediastinum have been known to give rise to benign and malignant tumors. Thus from connective tissue there may arise a fibroma, fibrosarcoma, myxoma and myxosarcoma; from vessels a lymphangioma, hemangioma and hemangiosarcoma; from muscle a leiomyoma and leiomyosarcoma; from fat a lipoma and liposarcoma; from nerve tissue a neurofibroma, neurofibrosarcoma, ganglioneuroma and sympathoblastoma; from connective, fat or reticular (histiocytic) cells a xanthoma; from the bony cage, from the tracheobronchial cartilages or from mesodermal elements as a result of metaplasia a chondroma, chondrosarcoma and osteochondroma; from congenitally misplaced tissue rests teratoid tumors and cysts; from aberrant thyroid tissue an adenoma and carcinoma, and from aberrant parathyroid tissue an adenoma. The only tumors, however, that are frequent enough to warrant further consideration are lipomas, neurogenic neoplasms, teratoid growths and cysts, and mediastinal goiter.

Lipomas.—Mediastinal lipomas are uncommon tumors, there having been less than fifty cases recorded in the literature. They have been observed at all ages and have no predilection for either sex. *Symptoms*, depending entirely upon the location and size of the tumor, are of as many as twenty years' duration. They are those of any mediastinal tumor namely pain, dyspnea, or cough. Mediastinal lipomas may be conveniently divided into three main groups: (1) the *hour-glass type* wherein one portion of the tumor is extra-thoracic, another part intra-mediastinal and a third sector consisting of a narrow connecting stalk is intramural. The diameters of the bullous portions measure as much as 15 cm. across. The extra-thoracic segment is found laterally, anteriorly or posteriorly, the intramural part perforates between the ribs and the intra-thoracic portion is located anywhere within the mediastinum, (2) *superior mediastinal* whence it extends to the base of the neck either in the midline or laterally and (3) entirely *intra-thoracic*. Since the latter are not palpated externally they do not attract attention until they produce symptoms by compressing the mediastinal structures. Consequently tumors measuring as much as 25 cm. in diameter and weighing 17½ lbs. have been recorded. *Grossly*, lipomas here as elsewhere are soft, well encapsulated and light yellow. *Histologically*, they are composed of adult fat cells. A *diagnosis* of lipoma of the mediastinum is usually not made preoperatively, although it should be suspected if roentgenograms disclose a tumor mass with a decreased peripheral opacity. *Treatment* is surgical excision. The *prognosis* is good.

Neurogenic Neoplasms.—These constitute the third most common group of mediastinal tumors being exceeded only by teratoid

and thyroid growths. They arise from intercostal or less often other nerves and from the sympathetic ganglia. They affect females more frequently than males, and are found at all ages, although more than one half of those arising from ganglia are present in children under ten years of age. Neurogenic tumors are often asymptomatic and are discovered in routine roentgenograms of the chest. Clinical manifestations when present consist of pain, dyspnea, Horner's syndrome or those of spinal cord injury. Roentgenograms disclose a round or lobulated tumor usually situated in the most posterior portion of the superior mediastinum. Rib erosion may be present in growths attached to the intercostal nerves



FIG. 196—Ganglioneuroma showing a central encephaloid area of sympathoblastoma

while erosion of the transverse processes and bodies of the vertebrae often signifies a malignant transformation.

If carefully dissected the nerves from which the neoplasms arise can usually be found entering the tumor mass. As already stated, the growths are found in the region of the thoracic ganglia or along the intercostal or other nerves. They are usually well encapsulated, soft, firm or hard, and measure as much as 20 cm. in diameter. Their shape varies from globular, flat or lobulated to dumb-bell like wherein one portion of the tumor is intrathoracic and one is intraspinal. Cut surfaces are composed essentially of grey or white compact or somewhat myxomatous tissue. Rarely they may disclose irregular nodules of encephaloid or hemorrhagic tissue which represent foci of malignant transformation (Fig 196). *Histologi-*

cally, tumors arising from intercostal or other nerves are usually *neurofibromas* and differ in no way from similar neoplasms arising in peripheral nerves. They have already been considered in Chapter I. While neurofibromas may also arise in sympathetic ganglia, tumors of these structures usually present a more varied and unique histologic structure. This can be understood only if the *histogenesis* of *sympathetic ganglia* is borne in mind. The primitive cells are medullary epithelial, arising from neural crest cells, which give rise to sympathogonia or the mother cells. These produce three groups of cells: (1) neurilemma or Schwan cells which are the supporting structures, (2) sympathoblasts (neuroblasts) which differentiate into ganglion cells and (3) pheochromoblasts which mature into pheochromocytes. The latter are chromaffin cells and are characteristically found in the adrenal medulla and other para-

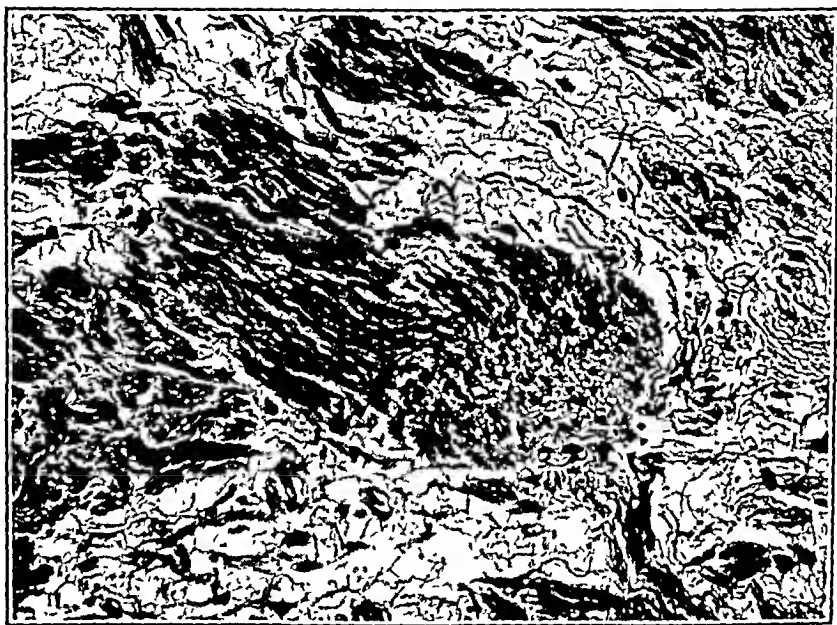


FIG 197.—Ganglioneuroma illustrating sections of nerve bundles. x 100.

ganglia rather than in sympathetic ganglia. Abnormally, tumors composed of each one of these cells have been described in sympathetic ganglia and what is more the cell types are rarely pure. This, of course, adds to confusion in classification which incidentally is rampant. Despite the number of possible variations there are only two tumors arising from sympathetic ganglia in the thorax that are of practical significance, namely ganglioneuroma and sympathoblastoma. *Ganglioneuroma* is composed of coarse or edematous fibrous tissue strands mixed with medullated or non-medullated nerves and containing varying numbers of ganglion cells (Fig. 197). These are large multipolar or ovoid cells with abundant eosinophilic or basophilic cytoplasm and often containing several round, relatively small, evenly stained eccentrically placed nuclei (Fig. 198). When the tumor undergoes a malignant transformation there is an addition of sympathoblasts. *Sympathoblastomas* have also been called sympathicoblastomas and neuroblastomas. They

are locally invasive and metastasize. Their cells are small, round and resemble lymphocytes. The cytoplasm is scanty, the nuclei are evenly and deeply stained, and the cellular arrangement is diffuse with often a tendency to rosette formation (Fig 199). These tumors may contain nerve fibers in varying numbers.

A clinical *diagnosis* of a neurogenic tumor is suggested only by demonstrating roentgenographically a sharply circumscribed tumor mass in the extreme posterior portion of the superior mediastinum or between the ribs. *Treatment* is complete surgical excision. *Complications* of a neurofibroma and ganglioneuroma consist of a malignant transformation usually into a neurofibrosarcoma and a sympathoblastoma respectively. If extirpated before this change has occurred, the *prognosis* is good.



FIG 198

FIG 199

FIG 198—Ganglioneuroma showing several ganglion cells set in an edematous connective tissue stroma $\times 200$

FIG 199—Sympathoblastoma. There is a poor attempt at rosette formation $\times 100$

Teratoid Tumors and Cysts—This group of mediastinal neoplasms is second in frequency only to tumors of thyroid tissue. Because clinically teratoid growths differ somewhat from other mediastinal cysts, the two will be considered separately.

Although *teratoid tumors* are congenital in origin they are sometimes not discovered until the seventh decade of life. Eighty-two per cent, however, are diagnosed before the age of forty years and the majority of these are found in the third decade. They have no predilection for either sex and are asymptomatic until they become large enough to impinge upon adjacent organs or until complications arise. Some of the more common *symptoms* and *signs* are cough with or without sputum, pain in the chest that may radiate to the shoulders, dyspnea, loss of weight, palpitation, hoarseness, dysphagia, weakness, edema of the face and upper extremities, engorgement of the superficial veins, cyanosis and fever.

Roentgenograms of the chest show an opacity either in the superior portion of the mediastinum behind the sternum or one extending from this region into the right or left pleural cavity. Sometimes teeth or other osseous tissue may be demonstrated radiologically. Although these lesions are doubtlessly of embryologic origin, their *genesis* still remains a fertile field for speculation. Among others they have been considered to arise from parasitic fetal remains, ectodermal midline inclusions, misplaced thyroid tissue, thymus, trachea, bronchi and the third and fourth branchial arches. Cogent arguments have been advanced for most of these theories and it is

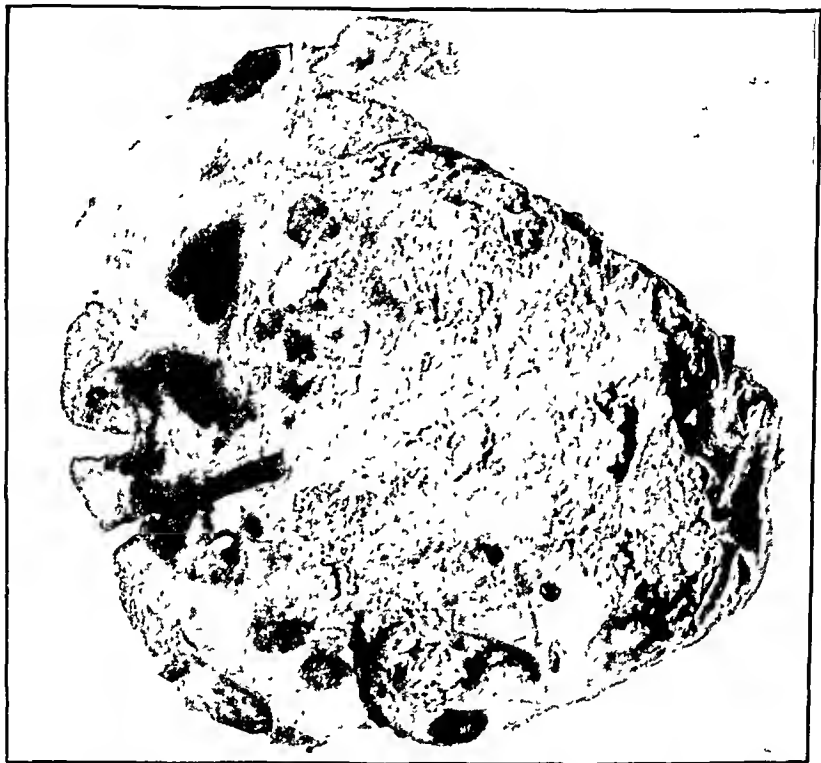


FIG 200 —Malignant teratoma of the mediastinum The tumor is solid and discloses sebaceous material, cartilage and necrotic tissue.

possible that none explains the origin of all the tumors, but that each accounts for the genesis of some of them.

Confusion also abounds with regards to the *pathologic* classification due undoubtedly to their varied histologic composition and to the fact that transitions from one type to another are frequent and subtle. Depending upon the parent tissues involved, they may nevertheless be divided into three main categories, (1) *epidermoid cysts*—composed entirely of ectodermal tissue, (2) *dermoid cysts*—composed of ectodermal and mesodermal tissues and (3) *teratoma*—composed of ectodermal, mesodermal and entodermal tissues. *Grossly*, as already stated, they are usually found in the upper and anterior portion of the mediastinum but occasionally they extend inferiorly to as low as the diaphragm and, perhaps more frequently, they protrude to one side or the other to fill most of the thoracic cavity. Even in such cases the tumors have a pedicle that connects

them with the mediastinum. The size varies from several to 15 or 20 cm in diameter. The external surface is usually smooth and rounded or bossed, but it may be less well-defined and densely adherent to the pericardium, great vessels, lungs, bronchi, trachea, chest wall or sternum. On section the epidermoid cyst is unilocular but it may contain partial partitions or ridges. Its inner surface may be smooth or rough, and its lumen is filled with clear or milky fluid or greasy lardaceous material mixed with hair. Dermoid cysts are similar except that frequently their walls are thicker and they contain areas of solid tissue, while teratomas are mostly solid but may contain small cysts (Fig 200). *Histologically*, epidermoid cysts are lined with stratified squamous epithelium beneath which there are often sebaceous and sweat glands and through which hairs may pierce. Dermoid cysts disclose, in addition, connective tissue, cartilage, bone, bone marrow and muscle, whereas teratomas contain any of these elements together with portions of the digestive tract including liver and pancreas, portions of the respiratory tract, thyroid tissue or thymus gland. Epidermoid cysts are as frequent as the other two combined.

In the absence of complications a diagnosis of a teratoid tumor can be made only radiologically by demonstrating bone or teeth in a tumor situated in the anterior portion of the superior mediastinum. If the lesion is suspected, needle aspiration of sebaceous material or hair through the chest wall clinches the diagnosis. Sometimes nature accomplishes a similar feat when the tumor ruptures into the trachea or a bronchus resulting in expectoration of hair and lardaceous material. Other complications which may arise are rupture into the pericardium, pleural cavity, aorta or vena cava and a malignant transformation. The latter occurs in about 13 per cent of all cases and is more frequent in the solid tumors. The only effective treatment is complete surgical excision. This should be performed as soon as the lesion is discovered because it is successful only before dense adhesions are formed and before a malignant change supervenes.

In contrast to teratoid tumors other mediastinal cysts are rare. The most common are bronchial cysts also called bronchogenic cysts, ciliated columnar epithelial cysts and reduplication cysts of the respiratory tract. They probably arise as a pinching off of the entodermal tube at the time of the division of the trachea and esophagus. They are located anywhere along the trachea and bronchi but are most frequent in the posterior part of the superior mediastinum at the tracheal bifurcation. They are round or oval, are externally smooth, have no attachment to the trachea or bronchi, vary in size and are filled with clear viscid or gelatinous fluid (Fig 201). *Histologically*, they are lined with ciliated pseudostratified columnar epithelium sometimes interspersed with areas of squamous epithelium and they contain within their fibrous tissue walls glands, cartilage, smooth muscle, nerves and elastic tissue (Fig 202). These cysts have been discovered at all ages, affect both sexes with equal frequency and are usually asymptomatic. Occasionally, however, they may produce pain, cough, emphysema and dysphagia.

Treatment consists of complete surgical excision. *Gastroenteric* cysts arise similarly to bronchogenic cysts. They are located in the posterior mediastinum behind the trachea and esophagus and along the vertebrae. They are adherent to the esophagus, lung or diaphragm, may erode the vertebrae, vary in size, are unilocular, and contain clear amber turbid or sanguineous fluid. *Histologically*, they resemble the stomach or some portion of the small intestine. All reported cases have been in children under ten years of age, and symptoms when present are those of pressure upon the trachea bronchi and esophagus. Treatment is surgical excision. *Pericardial celomic cysts* are also developmental and arise from faulty fusion of the multiple lacunae from which the pericardium is formed.



FIG. 201

FIG. 202.

FIG. 201.—Bronchial cyst

FIG. 202.—Bronchial cyst showing a lining of pseudostratified columnar epithelium and regular glands within its wall. x 50.

If separation is incomplete the result will be a diverticulum, but if it is complete there will form a cyst. This is found in the anterior mediastinum in contact with the pericardium, thoracic wall, diaphragm or pleurae. It varies in size, has a thin wall and is filled with clear fluid. *Histologically*, it is composed of thin connective tissue lined with a single layer of mesothelial cells.

Mediastinal Goiter.—This is the most common benign tumor of the mediastinum. Most if not all of the intrathoracic goiters arise as adenomas of the isthmus or lateral lobes of the thyroid gland. It has been stated that from 0.25 to 10 per cent of all adenomatous goiters descend into the mediastinum. This *migration* is possible because the thyroid is situated between two anatomic planes—the prevertebral and the pretracheal fascias—without a definite inferior

barrier Its descent into the thorax is facilitated by breathing, swallowing, muscular activity and gravity Its position is usually lateral, occasionally anterior and rarely posterior to the trachea (Fig 203) The mass is most frequently a circumscribed adenoma that varies greatly in size and that differs in no way from an adenoma of the thyroid located in the usual position It is well-encapsulated, is usually of the colloid type, and may show necrosis, hemorrhage, cystic degeneration or calcification Many of the patients are *symptomless* until the tumor becomes large enough to obstruct the trachea and great vessels The former results in dyspnea, choking, or stridor, whereas the latter produces dilatation of the veins of the upper portion of thorax and neck *Complications* that may develop consist of thyrotoxicosis which is said to occur in as many as 50 per cent of all cases, complete tracheal obstruction and suffocation sometimes precipitated by an otherwise harmless tracheitis, and a cancerous transformation which is found in about 3 per cent of the cases *Treatment*, therefore, even in the absence of symptoms is complete surgical excision

Mechanical Disturbances — The most common mechanical disturbance in the soft tissues of the mediastinum is the presence of a tumor mass either primary or secondary that produces pressure upon vital structures This has already been referred to twice in the present chapter Of importance, but much less frequent, are *foreign bodies* which gain entrance as a result of automobile accidents, street fights, and warfare The penetrating objects, therefore, are quite varied Frequently, the lungs and pleural cavities, as noted in Chapter V, are also involved, but sometimes these escape and the mediastinal structures alone are implicated There may be immediate or delayed injury to the heart, great vessels, trachea, bronchi or esophagus Treatment, therefore, is removal of all such objects A third mechanical disturbance, and of little importance as far as the mediastinum itself is concerned, is *emphysema* Air gains entrance from the outside as a result of penetrating wounds, from the lungs by way of the interstitial tissues or as a complication of tracheotomy



FIG 203 — Mediastinal goiter descending behind the trachea and esophagus

AORTIC ARCHES

Formerly abnormalities of the thoracic aorta and its main branches were only of academic or medical importances, but with the advent of vascular surgery they are now as much a surgical as they are a medical problem. Their inclusion in a textbook such as this is, therefore, mandatory.

EMBRYOLOGY

Early in embryonic development there are *two primitive aortas*, each consisting of a ventral and a dorsal part which fuse before the third week to form respectively the aortic sac and the descending aorta (Fig. 204). Then, as a result, of the interposition of the pharynx with its pouches between the heart and

the aorta, there develops on each side a series of *six aortic arches* each appearing in its respective order from above down. Each arch is formed from two sprouts—one from the aortic sac and the other from the dorsal aorta. In fishes the arches persist giving branches to the gills, while in man parts disappear entirely and others are greatly modified. Thus in adult life what remains of the *first arch* forms the mandibular artery. The *second arch* forms the hyoid and stapelial arteries. The *third arch* near the aortic sac gives off a bud which later becomes the external carotid artery, while the part proximal to this bud becomes the common carotid artery and that distal becomes the internal carotid. The portions of the dorsal aortas between the third and fourth arches have in the meantime disappeared. On the left side, the *fourth arch* persists in its entirety forming the normal aortic arch. It incorporates the cephalic portion of the aortic sac and retains its connection with the fused dorsal aortas or what is now known as the descending aorta. Meanwhile the seventh cervical intersegmental arteries have joined the fourth arches, and they later become the subclavian arteries. On the right side, the dorsal portion of the fourth aortic arch between the entrance of the seventh cervical segmental artery (the future right subclavina) and the descending aorta disappears. The entire ventral portion of the fourth arch

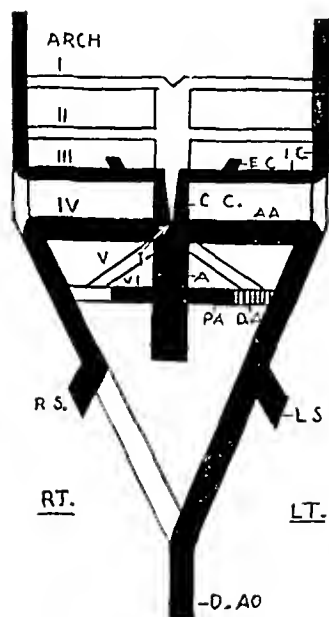


FIG 204 —Diagrammatic sketch of the aortic arches. Blocked areas represent the definitive arteries, unblocked areas those that disappear. I, II, III, IV, V and VI are the arches. E C —external carotid. I C —internal carotid. C C —common carotid. I —innominate. A A —aortic arch. A —aortic sac. P.A.—pulmonary artery. D A —ductus arteriosus. R.S.—right subclavian. L.S.—left subclavian. D.Ao —descending aorta.

thus becomes the right subclavian artery. The aortic sac where the fourth arch joins the right common carotid artery then elongates forming the innominate artery. The *fifth arches* are transitory and do not contribute to any permanent branches. The proximal por-

tions of the sixth arches become the pulmonary arteries whereas the distal portion on the right side disappears entirely and that on the left becomes the ductus arteriosus

PATHOLOGY

Congenital Anomalies—Development malformations of the fourth and sixth aortic arches are the most significant. They consist of coarctation of the aorta, patent ductus arteriosus, posterior right subclavian artery, right sided aortic arch, double aortic arch and stenosis or atresia of the pulmonary artery.

Coarctation of the Aorta—Coarctation of the aorta is a partial or complete constriction of the aorta directly opposite, above or below the entrance of the ductus arteriosus or the ligamentum arteriosum. It occurs in from 0.05 to 0.13 per cent of all patients coming to necropsy. Symptoms may be few, varied, or entirely absent. When present they are usually those of hypertension and include precordial pain, headache, dizziness and epistaxis or they are those of cardiac failure. Physical signs consist of combinations of left sided cardiac enlargement, systolic and less often diastolic murmurs heard at the level of the second intercostal space just lateral to the sternum and often transmitted to the neck, hypertension in the upper and hypotension in the lower extremities, and visible or palpable pulsations of the internal mammary, the intercostal, the carotid, the deep epigastric and the medial scapular arteries. Roentgenographically, there may be left ventricular enlargement, slight dilatation of the ascending aorta, erosion of the inferior margins and posterior portions of the ribs, and direct visualization of the constriction following intravenous injection of diodrast.

Pathologically, the constriction is usually within 1 cm. of the entrance of the ductus arteriosus or ligamentum arteriosum and, as already stated, the narrowing may be slight or the aorta may be represented by a fibrous cord (Fig. 205). Sometimes the constriction involves the origin of the left subclavian artery and rarely that of the right (if it is anomalous) in which case the blood pressures in the arms would vary. The ductus arteriosus is patent in only 13 per cent of all cases. The degree of development of a *collateral circulation* depends directly upon the degree of stenosis. It is established by the anastomosis of vessels arising from the aorta above the constriction with branches of the aorta below the constriction. These consist of (1) the intercostal, musculophrenic and pericardiophrenic, and the superior epigastric branches of the internal mammary artery anastomosing respectively with the aortic intercostal, the inferior phrenic of the abdominal aorta, and the deep epigastric from the iliac arteries, (2) the superior intercostal artery from the subclavian with the first aortic intercostal artery, (3) the descending branch of the transverse cervical with the posterior branches of the aortic intercostal arteries and (4) the highest thoracic, the pectoral branches of the thoricoacromial and the lateral thoracic from the axillary artery anastomosing freely with the lateral branches of the aortic intercostals along the lateral side of the chest wall.

An unequivocal positive *diagnosis* can be rendered upon demonstrating hypertension in the upper extremities and hypotension in the lower ones, upon showing the notchings along the inferior costal margins radiographically and upon visualizing the constriction angiocardigraphically. Heretofore, *treatment* was medical, but since it has been conclusively demonstrated that the constricted segment can be successfully resected and an end to end anastomosis of the aorta performed, the treatment, henceforth, will doubtlessly be surgical. In view of the newness of the latter therapy the *prognosis* in the future is still unpredictable. In medically treated patients, however, it varies. Some die in infancy while a few live to old age. It depends upon the degree of stenosis, the development



Anterior

Posterior

FIG 205 —Coarctation of the aorta at C L A —ligamentum arteriosum. L P.—left pulmonary artery. R.P.—right pulmonary artery. P —main pulmonary artery. A A.—ascending aorta with rupture R —in posterior view. I.—innominate artery. L C C —left common carotid artery. L S —left subclavian artery. D A.—descending aorta.

of a collateral circulation, and the amount of physical effort. The causes of *death* are cardiac failure, cerebral hemorrhage, rupture of the ascending aorta in the presence or absence of an aneurysm, and streptococcus viridans endarteritis at the site of the lesion.

Patent Ductus Arteriosus.—The function of the ductus arteriosus is to shunt the blood from the pulmonic to the aortic circulation during intra-uterine life. Postnatally it has no function and it is completely obliterated within the first eight weeks of life in 88 per cent of cases and at the end of the first year in 95 per cent of cases. Some of the remainder obliterate thereafter, but a few retain their patency throughout life. In these patients *symptoms* referable to the defect may not become apparent until after the fourth year. They may consist of retardation of growth, of those resulting from cardiac failure and of those consequent to a streptococcus viridans

pulmonic arteritis. Physical examination discloses a large heart, a thrill over the precordium, a low machinery-type of murmur over the pulmonic area, an accentuated second pulmonic sound and sometimes a water-hammer type of pulse. Roentgenographically, there may be cardiac enlargement, a prominent pulmonary conus which shows increased pulsation fluoroscopically, pulmonary congestion

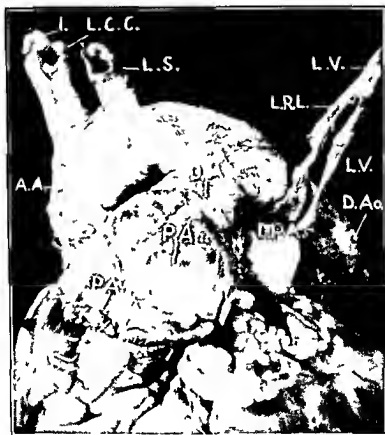
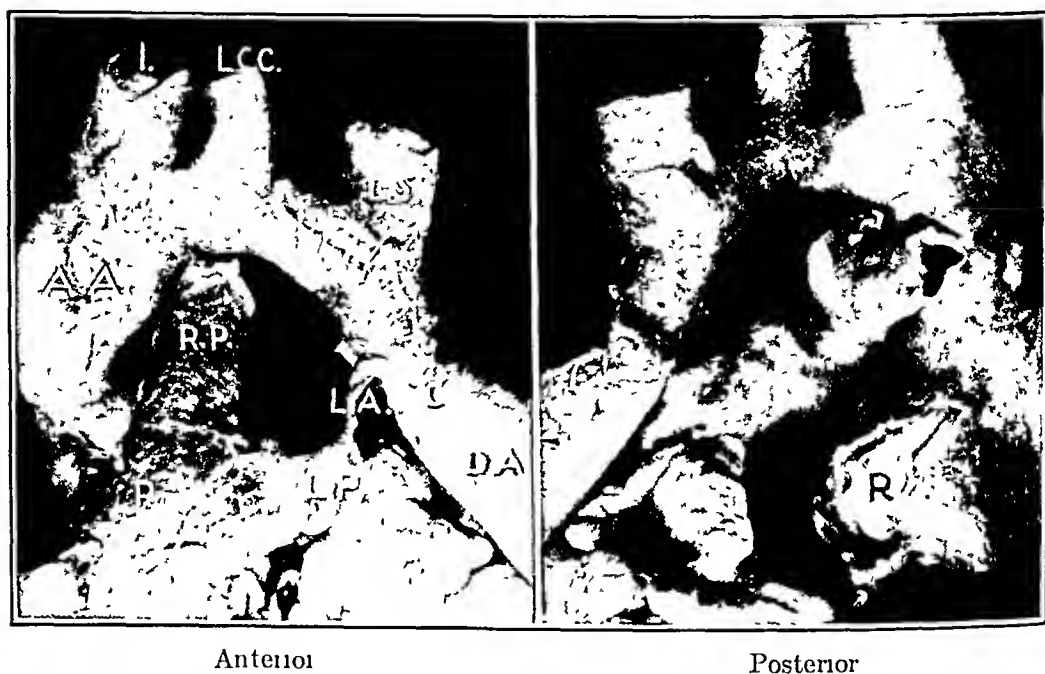


FIG 206 —Patent ductus arteriosus—DA PA—a dilated pulmonary artery PAn—large calcified aneurysm LPA—left pulmonary artery AA—ascending aorta I—inominate artery LCC—left common carotid artery LS—left subclavian artery D Ao—descending aorta LV—left vagus nerve LRL—left recurrent laryngeal nerve

and edema, and occasionally, calcification of the ductus or pulmonary artery.

The size of the ductus arteriosus varies considerably. It may be so short and stubby that there is virtually only an opening between the pulmonary artery and aorta, or it may be 3 cm long. Until about the twentieth year of life, it is pliable, but after that age it frequently becomes rigid and partly or completely calcified. The pulmonary artery is usually dilated at times to such a degree that its wall is paper thin, it may rupture, or it may form an aneurysm which in turn may rupture or become calcified (Fig 206). Infection with streptococcus viridans is quite common. In such cases, small, warty, friable, internal vegetations are found upon the pul-

An unequivocal positive *diagnosis* can be rendered upon demonstrating hypertension in the upper extremities and hypotension in the lower ones, upon showing the notchings along the inferior costal margins radiographically and upon visualizing the constriction angiocardiographically. Heretofore, *treatment* was medical, but since it has been conclusively demonstrated that the constricted segment can be successfully resected and an end to end anastomosis of the aorta performed, the treatment, henceforth, will doubtlessly be surgical. In view of the newness of the latter therapy the *prognosis* in the future is still unpredictable. In medically treated patients, however, it varies. Some die in infancy while a few live to old age. It depends upon the degree of stenosis, the development



Anterior

Posterior

FIG. 205 —Coarctation of the aorta at C. L.A.—ligamentum arteriosum. L.P.—left pulmonary artery. R.P.—right pulmonary artery. P.—main pulmonary artery. A.A.—ascending aorta with rupture. R.—in posterior view. I.—innominate artery. L.C.C.—left common carotid artery. L.S.—left subclavian artery. D.A.—descending aorta.

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pulmonic arteritis. Physical examination discloses a large heart, a thrill over the precordium, a low machinery-type of murmur over the pulmonic area, an accentuated second pulmonic sound and sometimes a water-hammer type of pulse. Roentgenographically, there may be cardiac enlargement, a prominent pulmonary conus which shows increased pulsation fluoroscopically, pulmonary congestion



FIG 206—Patent ductus arteriosus—D A P A—a dilated pulmonary artery P An—large calcified aneurysm L P A—left pulmonary artery A A—ascending aorta I—innominate artery L C C—left common carotid artery L S—left subclavian artery D A o—descending aorta L V—left vagus nerve L R L—left recurrent laryngeal nerve

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monic orifice of the ductus itself or covering the surface of the adjacent pulmonary artery (Fig. 207).

A *diagnosis* of patent ductus arteriosus is made upon discovering a continuous machinery-type of murmur heard over the pulmonic area and upon visualizing radiologically a prominent pulsating pulmonary conus. *Treatment* is surgical ligation with or without division of the vessel. This should be carried out prophylactically as soon as the diagnosis is made. In such cases the *prognosis* is good.

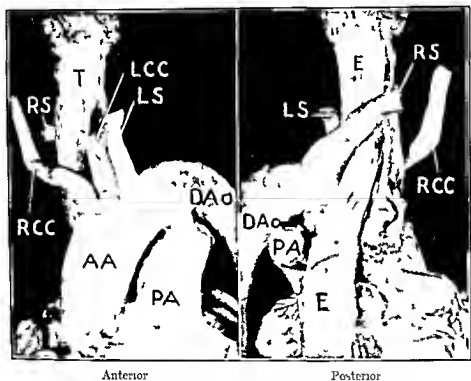


FIG. 207.—Patent calcified ductus arteriosus that ruptured during surgical ligation. P.A.—opened pulmonary artery. C.—pulmonic opening of the ductus arteriosus D.A. Both C and P.A. disclose several intimal vegetations caused by a streptococcus viridans infection.

In the absence of surgical therapy three-quarters of the patients are dead by the age of forty years from streptococcus viridans endarteritis, from congestive heart failure or from rupture of the pulmonary artery.

Posterior Right Subclavian Artery.—Both the right seventh cervical intersegmental artery and the anterior portion of the fourth aortic arch between the entrance of this vessel and the aortic sac normally form the right subclavian artery. Occasionally, the posterior portion of the fourth arch is utilized while the anterior portion disappears. In such cases, the definitive right subclavian artery originates as the last branch of the aortic arch, and usually reaches the right side by crossing behind the esophagus. The incidence of

this anomaly is reported as varying from 1 in 50 to 1 in 250 cadavers. As a rule, there are no accompanying signs and symptoms, but occasionally there may be dysphagia, vomiting, loss of weight, cyanosis, inequality of the radial pulse, pressure upon the thoracic duct or trophic changes in the upper extremity. Radiologically, a barium filled esophagus usually reveals a defect about 0.5 cm in width which passes obliquely from left to right behind the esophagus just above the level of the aortic arch. The artery, as already stated, most often arises as the last branch of the aortic



Anterior

Posterior

FIG 208—Posterior right subclavian artery. AA—ascending aorta. RCC—right common carotid. LCC—left common carotid. LS—left subclavian. RS—right subclavian. DAo—descending aorta. PA—pulmonary artery. T—trachea. F—esophagus.

arch just distal to the left subclavian artery, but sometimes it makes its exit directly opposite the latter vessel (Fig 208). In 80 per cent of the cases its subsequent course is between the esophagus and the vertebrae, whereas in 15 per cent it is described as passing between the trachea and esophagus and in 5 per cent as traversing anterior to the trachea. The latter two positions are more difficult to explain embryologically. Normally, the right recurrent laryngeal nerve winds around the subclavian artery as it emerges from the innominate artery. When the subclavian vessel is anomalous the nerve is usually replaced by branches which pass directly to the larynx and less often it winds around the inferior thyroid artery or the right vertebral artery. *Treatment* is rarely necessary, but when there is accompanying dysphagia with progressive loss of weight it

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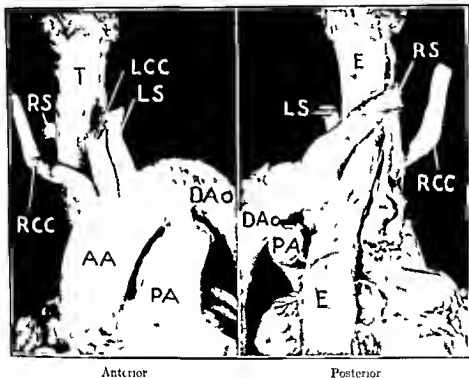


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Anterior

Posterior

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consists of surgical ligation and severance of the main trunk near its exit from the aorta. The distal end then retracts to the right side of the esophagus.

Right-Sided Aortic Arch.—In these cases the right fourth aortic arch persists as the definitive arch, whereas the left one partially disappears. Its incidence is recorded as varying from 1 in 158 to 1 in 1400 autopsies. This anomaly is usually asymptomatic until later life when a dilated and tortuous sclerotic aorta may produce pressure upon the esophagus, trachea or recurrent laryngeal nerve.

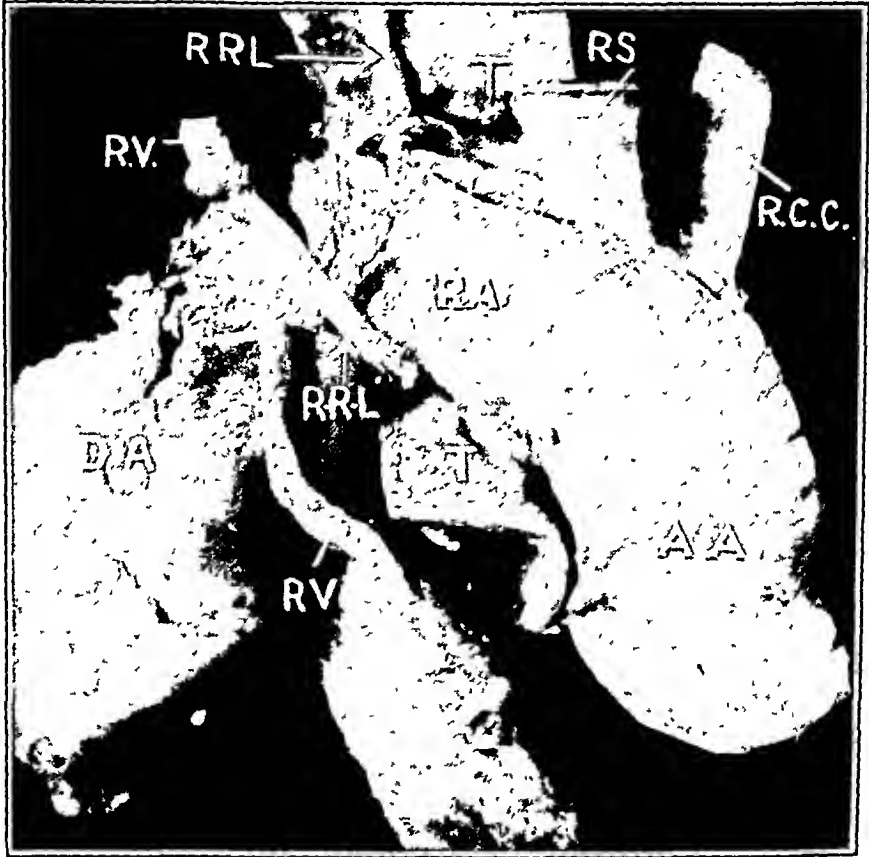


FIG. 209.—Right aortic arch. Right lateral view. A.A.—Ascending aorta. R.A.—right aortic arch. D.A.—descending aorta. R.C.C.—right common carotid. R.S.—right subclavian. T.—trachea. R.V.—right vagus. R.R.L.—right recurrent laryngeal nerve. (Herbut Arch Path)

Symptoms that have been described are dysphagia, stridor, hoarseness, cough, pain in the chest and a tingling sensation in the left arm. Bronchoscopic and esophagoscopy examinations may disclose a pulsating tumor indenting the walls of the trachea and esophagus from the right; a fluoroscopic examination shows a pulsating aorta to the right of the trachea; roentgenograms of a barium filled esophagus disclose a concave depression to the right and posteriorly, and an angiocardigram permits direct visualization of the aortic arch to the right of the trachea.

The ascending aorta either pursues its normal course, or it may be displaced somewhat to the right (Fig. 209). The arch curves above the hilum of the right lung and to the right of the trachea.

and esophagus. The descending aorta then crosses the midline posterior to the esophagus either immediately or obliquely before it passes through the diaphragm. The position of the left subclavian artery varies (fig 210). In one-third of the cases it arises

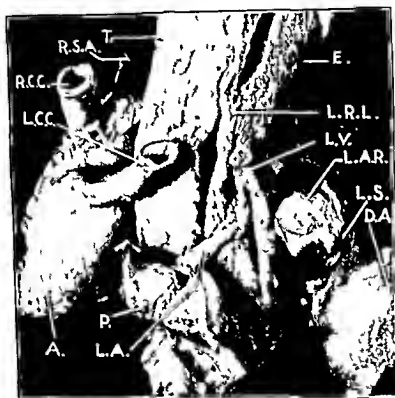


Fig 210—Right aortic arch. Left lateral view showing a left aortic root—I.A.R. to the tip of which is attached the ligamentum arteriosum—I.V.—P—pulmonary artery, A—ascending aorta, L.C.C.—left common carotid artery, R.C.C.—right common carotid artery, R.S.A.—right subclavian artery, L.S.—left subclavian artery, D.A.—descending aorta, L.V.—left vagus nerve, L.R.L.—left recurrent laryngeal nerve, E—esophagus, T—trachea.

from a left innominate artery whereas in two-thirds of the cases it arises posteriorly either as the last branch of the right aortic arch or from a persistent left aortic root. In my case there is no right innominate artery for the right common carotid artery and the right subclavian artery arise directly from the right arch. When the left subclavian artery arises from a left innominate, the ligamentum arteriosum is found in the usual location but on the r

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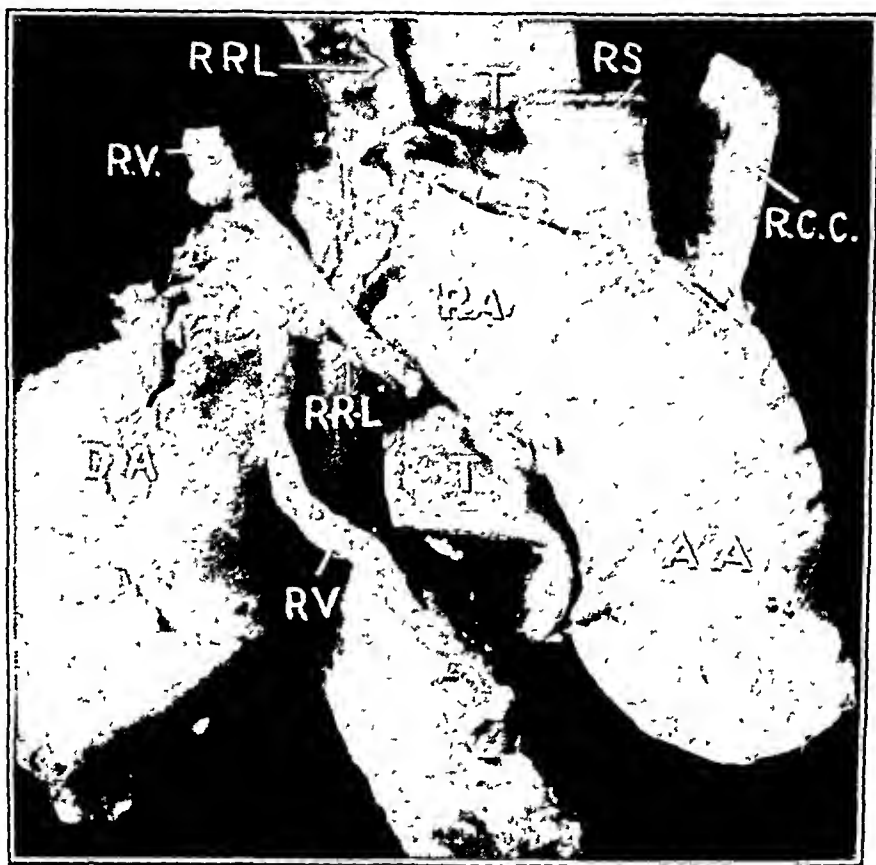


FIG. 209 —Right aortic arch Right lateral view A.A.—Ascending aorta. R A —right arch. D A.—descending aorta. R.C.C.—right common carotid R S.—right subclavian. T—trachea R.V.—right vagus R R L.—right recurrent laryngeal nerve. (Herbut Arch. Path.)

Symptoms that have been described are dysphagia, stridor, hoarseness, cough, pain in the chest and a tingling sensation in the left arm. Bronchoscopic and esophagoscopy examinations may disclose a pulsating tumor indenting the walls of the trachea and esophagus from the right; a fluoroscopic examination shows a pulsating aorta to the right of the trachea; roentgenograms of a barium filled esophagus disclose a concave depression to the right and posteriorly, and an angiocardigram permits direct visualization of the aortic arch to the right of the trachea.

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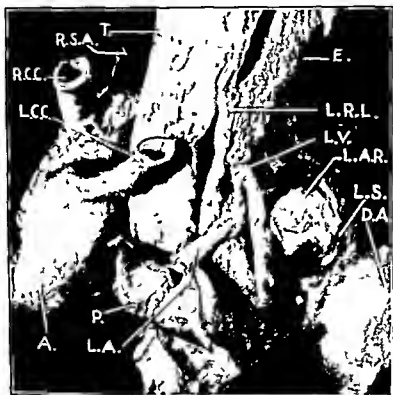
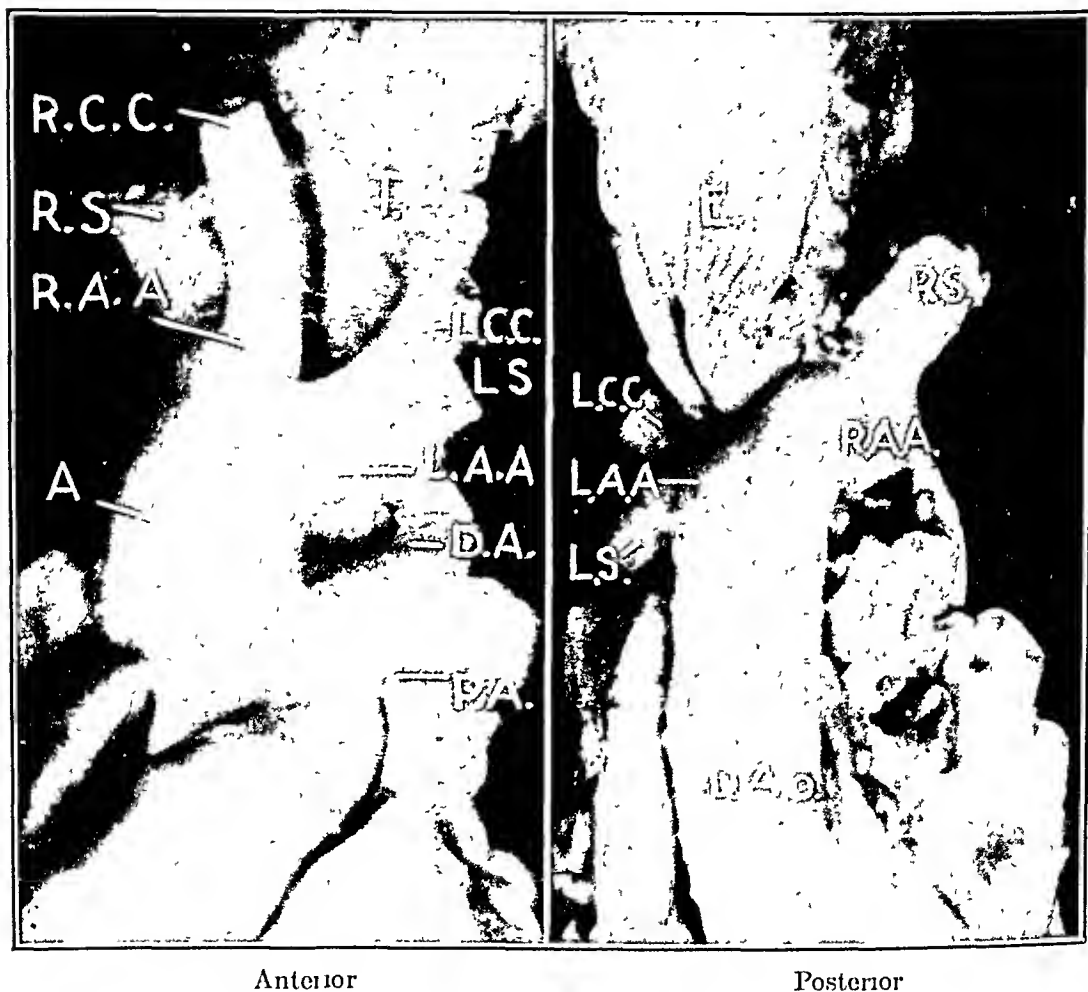


FIG 210—Right aortic arch. Left lateral view showing a left aortic root—I.A.R. to the tip of which is attached the ligamentum arteriosum—L.A. P—pulmonary artery. A—ascending aorta. L.C.C.—left common carotid artery. R.C.C.—right common carotid artery. P.S.A.—right subclavian artery. L.S.—left subclavian artery. D.A.—descending aorta. L.V.—left vagus nerve. I.R.L.—left recurrent laryngeal nerve. E—esophagus. T—trachea.

from a left innominate artery, whereas in two-thirds of the cases it arises posteriorly either as the last branch of the right aortic arch or from a persistent left aortic root. In any case, there is no right innominate artery for the right common carotid artery and the right subclavian artery arise directly from the right arch. When the left subclavian artery arises from a left innominate, the ligamentum arteriosum is found in the usual location but on the right side. When the left subclavian artery arises posteriorly, it connects the tip of the persistent left aortic root or the subclavian artery itself with the pulmonary artery. Occasionally, the entire left aortic arch, or its anterior portion in cases with a persistent left aortic root, remains as a fibrous cord. In all instances the right recurrent laryngeal nerve curves around the right aortic arch, whereas the left one winds around a left ligamentum arteriosum, when it is present, or around the left subclavian artery when it is absent.

Treatment is usually unnecessary. When pressure symptoms arise as a result of constriction from a completed but ligamentous left aortic arch, they may, however, be relieved surgically.

Double Aortic Arch.—This anomaly consists of a persistence of both the right and left fourth aortic arches. It is the least frequent of all arterial abnormalities in this region. Sometimes it produces no *symptoms* whatsoever as attested by observing the lesion in adults as an incidental finding at necropsy. At other times, and



Anterior

Posterior

FIG. 211.—Double aortic arch. A.—ascending aorta. L.A.A.—left aortic arch. R.A.A.—right aortic arch. R.C.C.—right common carotid. L.C.C.—left common carotid. R.S.—right subclavian. L.S.—left subclavian. P.A.—pulmonary artery. D.A.—ductus arteriosus. T.—trachea. E.—esophagus. D.Ao.—descending aorta. (Herbut & Smith, Arch. Otol)

so far described only in infants, it compresses both the trachea and esophagus resulting in dyspnea, stridor, difficulty in eating, cyanosis, cough, loss of weight, and susceptibility to pneumonia. Physical examination reveals nothing characteristic, although displacement of the trachea to the left and a tracheal tug have been described. Lateral roentgenograms of the thorax disclose narrowing and anterior displacement of the trachea at the level of the aortic arch, whereas a barium filled esophagus reveals a similar defect at the same level together with a bilateral indentation of its wall. Bron-

choscopy may show a constriction of the trachea just proximal to the carina, although frequently the patients are too ill to tolerate such an examination.

The *ascending aorta* is usually normal in size and position, and it bifurcates into a right and a left aortic arch just anterior to, or slightly to the right of, the trachea (Fig 211). As a rule, the right arch is of greater caliber than the left, but occasionally the reverse is true. The arches then pass lateral to the trachea and esophagus above the hilus of the corresponding lung, and unite posterior to the esophagus at the level of the fourth dorsal vertebra to form the descending aorta. There is no innominate artery. The first



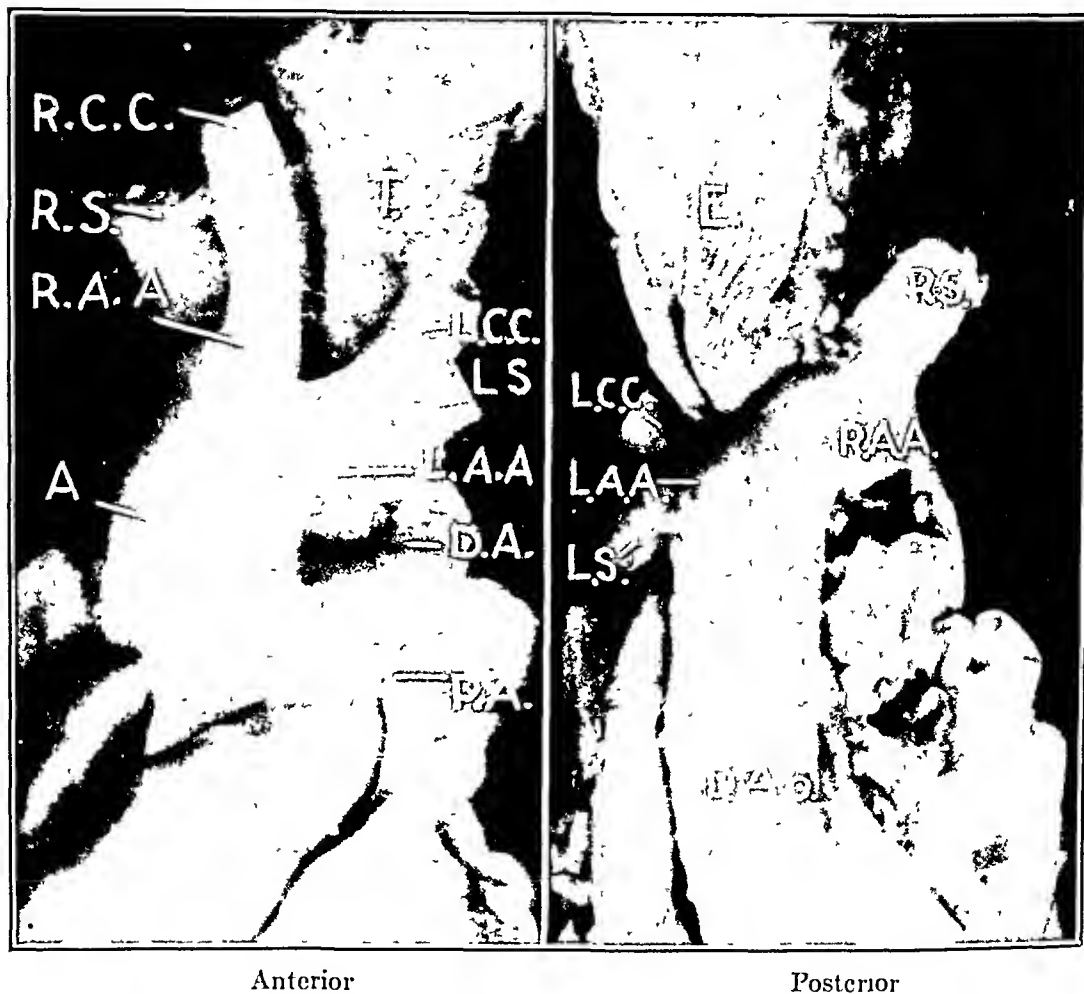
* FIG. 212—Tetralogy of Fallot showing a stenotic pulmonary artery, hypertrophy of the right ventricle and an applicator inserted through an interventricular septal defect into a deformed aorta.

branches arising symmetrically from the corresponding arch are the right and left common carotid arteries, and these are followed almost immediately by the right and left subclavian arteries. In all cases, the vagus and recurrent laryngeal nerves assume a symmetrical course in respect to their corresponding arches. Associated cardiac defects are not common.

A positive diagnosis of a double aortic arch can be made only radiologically. If the lesion produces progressively severe symptoms, the treatment is surgical severance of the constricting arterial collar. In the absence of accompanying signs and symptoms, however, surgical therapy is not indicated. The prognosis is excellent in asymptomatic cases, good in surgically treated patients, and poor

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Anterior

Posterior

FIG. 211.—Double aortic arch. A—ascending aorta. L.A.A.—left aortic arch. R.A.A.—right aortic arch. R.C.C.—right common carotid. L.C.C.—left common carotid. R.S.—right subclavian. L.S.—left subclavian. P.A.—pulmonary artery. D.A.—ductus arteriosus. T—trachea. E—esophagus. D.Ao—descending aorta. (Herbut & Smith, Arch. Otol.)

so far described only in infants, it compresses both the trachea and esophagus resulting in dyspnea, stridor, difficulty in eating, cyanosis, cough, loss of weight, and susceptibility to pneumonia. Physical examination reveals nothing characteristic, although displacement of the trachea to the left and a tracheal tug have been described. Lateral roentgenograms of the thorax disclose narrowing and anterior displacement of the trachea at the level of the aortic arch, whereas a barium filled esophagus reveals a similar defect at the same level together with a bilateral indentation of its wall. Bron-

evidenced by absence of pulmonary artery pulsations fluoroscopically, and radiologically, by an absence of the fulness of the pulmonary shadow, by a replacement of its normal convex shadow with a concave opacity, and by absence of evidence of pulmonary congestion. The immediate results following operation are excellent and consist of a decrease in cyanosis, decrease in dyspnea, increase in tolerance to exercise, a decrease in erythrocyte count, and a gradual disappearance of the clubbing of the digits. This method of therapy is too recent to properly evaluate the long range results for the operation produces an artificial ductus arteriosus and thus in itself, as already pointed out, is attended by complications of its own. Thus far, however, there has been no evidence of cardiac failure or of streptococcus endarteritis.

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in surgically untreated patients who present obstructive disturbances.

Stenosis or Atresia of the Pulmonary Artery.—This abnormality constitutes one of the more common vascular anomalies of the mediastinal arteries. It is usually discovered in infants or children, and while some patients reach adulthood the majority die far short of the normal span of life. *Signs and symptoms* consist of cyanosis, intolerance to exercise, clubbing of the fingers and toes, polycythemia, a systolic murmur and thrill in the second interspace just to the left of the sternum, an abnormal right axis deviation of the heart in electrocardiograms, and, radiologically, a small pulmonary artery. In its typical form, this lesion constitutes the *tetralogy of*

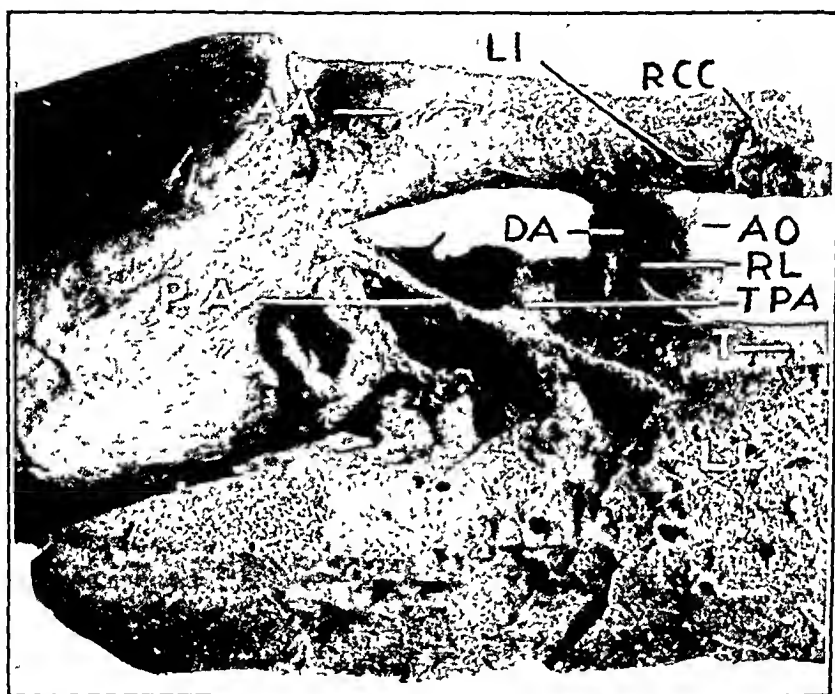


FIG. 213—Atresia of the pulmonary artery—left lateral view. A.A.—ascending aorta. R C C—right common carotid. L I—left innominate A.O.—right aortic arch D.A.—ductus arteriosus. R.L.—right recurrent laryngeal nerve T.P.A.—transverse pulmonary arch P.A.—atretic pulmonary artery. L L—Left lung. (Herbut & Fox, Am. Heart Jour.)

Fallot. This consists of stenosis of the origin of the pulmonary artery, interventricular septal defect, dextroposition of the aorta so that it straddles the septum, and hypertrophy of the right ventricle (Fig. 212). Sometimes the pulmonic artery is atretic, in which case life is maintained only by a patent ductus arteriosus or hypertrophied bronchial arteries (Fig. 213).

Because the ill-effects are due to a lack of oxygenation of the blood resulting from an insufficient pulmonic circulation and because the prognosis is otherwise poor, the current method of *treatment* is diverting some of the systemic circulation through the lungs. This is accomplished by anastomosing the innominate or the left subclavian artery to the right or left pulmonary artery. The indication for operation is a lack of blood flow through the lungs as

Chapter VIII

MOUTH, PHARYNX AND SALIVARY GLANDS

MOUTH AND PHARYNX

EMBRYOLOGY

THE mouth is formed by an invagination of the ectoderm that lies between the expanding brain and bulging pericardium. It is known as *stomodaeum*. Initially, it ends as a blind pouch and is separated from the anterior portion of the foregut by the buccopharyngeal membrane. The latter, however, disappears about the third week of embryonic life leaving, in the adult, no trace of its previous existence. Further development of the upper portion of the digestive tract may be briefly considered under the following five headings, jaws, teeth, tongue, tonsil and pharynx proper. The jaws are formed from a fusion of a series of mesodermal processes. The lower jaw—the simpler of the two—arises from the union of the first pair of branchial or the mandibular arches. The formation of the upper jaw is more complicated. It arises from derivatives of the frontonasal process that fuse with the maxillary processes. The latter arise as triangular outgrowths from the cephalic side of the dorsal end of the mandibular arches. The frontonasal process consists of a thickening of mesoderm between the floor of the fore-brain and the roof of the mouth. It gives rise to two lateral nasal processes and a median nasal process. The latter, in turn, gives rise to two globular processes. With growth of the head, the maxillary processes fuse first laterally with the lateral nasal processes and then medially with the globular processes. Meanwhile the globular processes have united not only with the lateral nasal processes but also with each other thus completing the formation of the upper jaw. At about the seventh week of embryonic life, a primary labial and then a secondary alveololabial groove separates the jaw into an anterior lip and an immediately posterior alveolus. At approximately the sixth week of life, the inner portions of the maxillary process give rise to the palatine processes which fuse across the mid-line with each other and with the lower border of the nasal septum. Their anterior portion remains membranous and persists as the soft palate. A tooth is a modified connective tissue papilla. The covering enamel comes from the epidermis, while the pulp dentine and cementum are derived from the mesoderm. The tongue develops from the ventral portions of the branchial arches and consists of an oral and a pharyngeal portion. The former arises from the mandibular or first arches anterior to the buccopharyngeal membrane, is covered with ectoderm, contains papillae, and is concerned with mastication. The pharyngeal portion or root is derived from the second arches but also received additions from the third and fourth. It is covered with endoderm, contains lymphoid tissue and is con-

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skin. The nuclei of the superficial cells, however, shrink and degenerate but do not disappear, so that normally there is no keratinization (Fig 214). In the submucosa, there are papillae that also are similar to those in the dermis except that they are more delicate. In the posterior portion of the oral cavity there are collections of lymphoid tissue in the submucosa which reach their acme in the palatine tonsil. Throughout the tunica propria there are numerous tiny glands that secrete a liquid (saliva) which moistens the mucosa. One specific structure that should be mentioned is the taste bud.

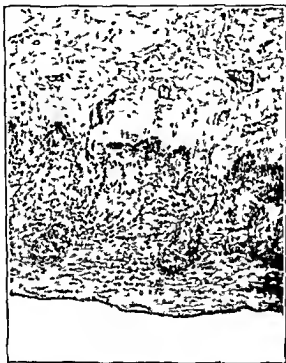


FIG 214—Normal buccal mucosa showing non keratinizing, squamous epithelium, delicate papillae, and a submucosa of fibrous tissue. $\times 50$

These are collections of neuro-epithelial cells that are particularly numerous on the sides of the circumvallate papillae and that are intimately connected with the terminal branches of the vagus nerves.

PATHOLOGY

Congenital Anomalies—Some developmental abnormalities of the mouth and pharynx are common whereas others are rare. They may be listed according to the organs affected: (1) *Lips* cheiloschisis—cleft lip, macrocheilia—enlargement, large frenum labii—associated with separation of the middle incisors. (2) *Oral opening* microstomus—large aperture, microstomus—small aperture, astomus—absence of opening. (3) *Tongue* ankyloglossia—tongue-tied due to short frenum, absence anterior portion, fusion with floor of mouth, bifid, trifold, lobulated, fissured, geographic—irregular map-

cerned with swallowing. The *tonsil* (palatine) appears at about the third month of embryonal life as a collection of lymphoid tissue at the site of the second pharyngeal pouch. The *pharynx* proper is a muscular tube that arises from the superior portion of the entodermal tube. It contains the branchial arches and pharyngeal pouches that develop into numerous and complex structures. Many of these have already been considered in this and previous chapters. The major *derivatives* consist of the soft palate, tympanic cavity, mastoid cells, root of the tongue, thyroid gland, tonsils, parathyroid glands, thymus, epiglottis and larynx.

ANATOMY

A detailed account of the buccal cavity and its structures is impossible in a book of this type. For more than a cursory survey, the reader is, therefore, referred to works on anatomy.

The mouth is divided into a vestibule and the mouth proper. The *vestibule* is the outer portion bounded by the lips, cheeks, gums and teeth. It receives the ducts of the parotid glands. The *mouth proper* is bounded by the hard and soft palate, gums, teeth and tongue and it communicates with the pharynx by way of the isthmus faucium. The temporary or deciduous *teeth* are 20 in number, and consist of 4 incisors, 2 canines and 4 molars in each jaw, while the permanent teeth are 32 in number and consist of 4 incisors, 2 canines, 4 premolars, and 6 molars in each jaw. The *tongue* consists of a root, a tip, a dorsum and an inferior surface. The root is pharyngeal in position and is attached to the hyoid bone and mandible. The dorsum is convex and contains a v-shaped groove, the sulcus terminalis, pointing to the foramen caecum and a series of papillae. The largest of these are the circumvallate papillae situated just anterior to the sulcus terminalis, while the fungiform and filiform papillae are scattered irregularly over the dorsal surface. The inferior surface is covered by a smooth membrane which is raised in the mid-line to form a frenulum. The *palatine tonsils* are two masses of lymphoid tissue located in the lateral walls of the oral part of the pharynx just opposite the root of the tongue. Each occupies the lower part of the sinus between the glosso-palatine and pharyngo-palatine arches, and the upper part of the sinus remains as the supratonsillar fossa. Other constant masses of lymphoid tissue appear in the posterior surface of the nasopharynx and are known as the *pharyngeal tonsils* or the adenoids. In addition, there are two collections of lymphoid tissue at the root of the tongue that are called the *lingual tonsils*. The *lymphatic drainage* of the buccal cavity is as follows: from the gums, teeth and lateral border of the tongue vessels empty into the submaxillary nodes; from the tonsil, hard palate and floor of the mouth into the superior deep cervical nodes; from the posterior part of the tongue into the jugulo-digastric and jugulo-omohyoid nodes, and from the soft palate and pharynx into the retropharyngeal nodes.

In general, the *mucous membrane* of the mouth is composed of stratified squamous epithelium that is similar to that seen in the

of unilateral cheiloschisis the palatine defect is also unilateral, but when the cleft lip is bilateral the deformity of the palate may be Y shaped with the common stem directed posteriorly. The cause of a median cleft lip is a lack of fusion of the two globular processes (which are derived from the median nasal process), and the cause of a lateral cleft lip is a failure of union of the maxillary processes with the globular processes. A continuation of each defect into the hard palate together with failure of fusion of the palatine processes (which are derived from the maxillary processes) are responsible for the clefts in the palate.

Based on a study of over 4,600 cases, it was the opinion of Warren B. Davis that these anomalies are familial in over 60 per cent of the cases, that they are rare in negroes and infrequent in Jews, and that there is rather commonly a concomitant absence of the lateral incisor teeth even on the contralateral side and in cases where the defect is minimal. *Symptoms* consist of difficulty in eating and later of impediment to talking. *Treatment* is surgical repair of the defects. The optimal time for operation on cleft lip is at three weeks to three months of age and on cleft palate at nine to twenty-two months. Proper treatment in the hands of an expert usually yields good results.

Inflammation—Inflammations of the mouth are known as *stomatitis*, of the gums as *gingivitis*, of the tongue as *glossitis*, of the tonsils as *tonsillitis*, and of the pharynx as *pharyngitis*. Strictly speaking many of these lesions are not surgical and, therefore, only a few of the more common and more pertinent infections will be considered.

Non-specific Inflammations—In this category will be included Vincent's infection, gangrenous stomatitis, Ludwig's angina, hairy tongue, tonsillitis, peritonsillar abscess and retropharyngeal abscess.

Vincent's infection of the mouth has also been called *ulcero-membranous stomatitis* and *gingivitis*, trench mouth, fusospirochaetosis, Plaut-Vincent's disease, phagedenic stomatitis and necrotic stomatitis. It is an acute contagious disease caused by the fusiform bacillus and Vincent's spirochaetes and characterized by ulcerations of the oral mucosa. Since these organisms are present in normal mouths, there must first be a lowering of resistance before they can gain a foot-hold. This often exists in the form of diabetes, vitamin deficiency, leukemia, faulty diet, poor dental hygiene, a break in the mucosa or a preceding streptococcal infection. As would be expected, therefore, the disease is common in jails, asylums, orphanages and army camps. *Symptoms* consist of pain, metallic taste, tenderness, bleeding from the gums and fever to 102°F. The lesions frequently begin along the free borders of the gums as edema of the interdental papillae. This is followed rapidly by necrosis, desquamation, and ragged, irregular ulcerations. Their floors are covered with a yellowish grey pseudomembrane which when removed leaves bleeding raw surfaces. From the gums, the lesions spread to the cheeks, lips, tongue, tonsils and other areas, although sometimes the primary site is extragingival. The *diagnosis* is made from the appearance and distribution of the lesions in the mouth coupled with the demonstration of myriads of fusiform bacilli and

like denudations of the papillae surrounded by hyperplastic epithelium, median rhomboid glossitis—a similar process producing a rhomboid area of bareness just anterior to the circumvallate papillae, macroglossia—enlargement seen in cretinism and mongolism, lingual thyroid, thyroglossal cyst. (4) *Jaws*: micrognathus—reduction in size, agnathus—absence often associated with congenital ectodermal dysplasia, contraction—narrowing, abstraction—widening, retrusion, protrusion, faulty occlusion. (5) *Teeth*: anodontia—absence, supernumerary, megadontismus—gigantism, microdontismus—diminution in size of crowns and roots, hypoplasia—diminution in size of either crowns or roots, dysplasia—defective formation, diastema—separation of the middle incisor teeth. (6) *Palate*—cleft, atresia of the soft portion. (7) *Pharynx*: branchial cysts—discussed in



FIG. 215 —Unilateral cleft lip and palate. (Courtesy Dr Warren B. Davis)

Chapter VI, diverticula—described in Chapter IX, stenosis, and atresia.

Cleft lip and palate are the most common and, surgically, the most important of all the aforementioned congenital anomalies. The former is *also known as* cheiloschisis and hare lip, and the latter as uranoschisis. Hare lip, named after the lip of the hare or rabbit, is a poorly chosen term, for in man the defect is usually lateral and not median, whereas in these rodents it is always in the midline. The flaw in the lip is of varying degrees from a mere notch to a complete separation that extends to and includes the nostril (Fig. 215). It is usually *unilateral* but it may be *bilateral*, and it may or may not be associated with a cleft palate. The latter defect is likewise variable. It may be partial, involving only the anterior or the posterior portion of the hard or soft palate respectively, or it may be complete, involving the entire palate. Usually it is associated with a cleft lip, but it may occur in patients with normal lips. In cases

cause of the enlargement of the papillae is unknown, although it is thought by some to be the result of a congenital predisposition and irritants such as syphilis tobacco and mouth washes. The condition is most frequent in men beyond forty years of age and as a rule produces no symptoms. When the villi become long, however, they have been known to produce tickling and gagging. In some the lesion disappears spontaneously. In others treatment is of no avail.

Tonsillitis is a common infection particularly in childhood. It is caused by the ordinary pyogenic bacteria that are found in the mouth, especially the streptococci. They gain entrance by way of a break in the epithelium of the crypts and are prone to grow and multiply in the presence of ill-health, overwork or faulty lymphatic drainage. In acute tonsillitis symptoms consist of a sudden onset of pain and dryness in the throat, fever to 105°F , dysphagia, head-

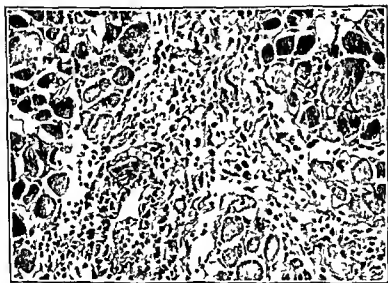


FIG. 216.—Ludwig's angina. There are edema of the intermuscular connective tissue and an infiltration with plasma cells lymphocytes and neutrophils. $\times 100$

ache, chilliness and general malaise. Pathologically, the tonsils (more commonly the palatine) are greatly enlarged, swollen, edematous, tender, red and are frequently covered with small flecks of exudate or with a grey pseudomembrane. The lymph nodes at the angle of the jaw are enlarged and tender. Since such tonsils are not removed surgically, one must resort to chance postmortem material for histologic studies. There are edema, congestion, and an infiltration with neutrophils, plasma cells and monocytes. With or without treatment symptoms usually regress in from three to five days and the patient completely recovers. Rarely, complications arise. These consist of otitis media, nephritis, arthritis, peritonsillar abscess (quinsy) or chronic tonsillitis. The latter encompasses a continuous low grade smouldering infection or repeated attacks of an acute infection that do not clear completely in the interim. There is al-

Vincent's spirochaetes in smears made from the ulcers. *Treatment* consists of relief of pain, local hygienic measures and the administration of sulfadiazine or penicillin. Surgical intervention of any kind is contraindicated.

Gangrenous stomatitis is also *known* as cancrum oris and noma. It is a rapidly spreading necrotizing and sometimes contagious infection of the mouth. The condition is practically confined to undernourished or sick children whose resistance has been lowered by illness such as pertussis, measles and scarlet fever, and to aged adults also suffering from debilitating diseases. *Local injuries* to the mucosa in the form of extraction of a tooth, biting of the cheeks and other trauma pave the way for the causative organisms—the microaerophilic streptococci, fusiform bacilli and Vincent's spirochaetes. The *lesion* usually appears near the angle of the mouth or opposite a molar tooth as a dark bluish red focus that quickly enlarges to produce a firm to ligneous infiltration with central necrosis and sloughing. The latter eventuates in exposure of underlying bones or complete destruction and perforation of the cheek. The odor is foul; salivation is excessive; prostration is the rule, and fever frequently reaches 106°F. *Treatment* consists of local applications of zinc peroxide, of antibiotic and chemotherapy, and, as advocated by some, radical surgical excision. The *prognosis* is grave for the mortality rate is as high as 90 per cent.

Ludwig's angina is a rapidly spreading phlegmonous infiltration of the floor of the oral cavity *caused* by any of the pyogenic organisms usually found in the mouth especially the streptococcus. The disease is almost always preceded by oral trauma, local stomatitis, caries, tonsillitis, peritonsillar or retropharyngeal abscess, otitis media or erysipelas of the face. Its greatest incidence is in young adult males. *There are* pain, fever, leukocytosis, dyspnea, dysphonia and dysphagia. *Grossly*, there is a tense, board-like swelling of the submental region that is usually situated above or below the mylohyoid muscles. With progression of the lesion the tongue is displaced upwards and backwards, and there is frequently edema of the larynx. Fluctuation is ordinarily not present, but in a few patients the tissue does break down to form abscesses. *Histologically*, there are congestion, edema of the connective and fat tissue, a perivascular and diffuse infiltration with neutrophils, lymphocytes, plasma cells and monocytes, and thrombosis and necrosis of the capillaries (Fig. 216). *Treatment* consists of antibiotic and chemotherapy and, when abscesses develop, of surgical drainage. *Complications* are suffocation, severe toxemia and thrombosis of the jugular veins. The duration of the disease is one to four weeks. With the advent of antibiotic and chemotherapy, the *prognosis* is good.

Hairy tongue is also *called* black hairy tongue, lingua villosa and lingua nigra. In its classical form it consists of a fur-like, brown or black discoloration of the posterior one-half of the dorsum of the tongue. The fur-like or hairy quality is due to a marked hypertrophy and hyperplasia of the filiform papillae, and the pigmentation is due to chromogenic bacteria, molds and fungi. The exact

cause of the enlargement of the papillae is unknown, although it is thought by some to be the result of a congenital predisposition and irritants such as syphilis, tobacco and mouth washes. The condition is most frequent in men beyond forty years of age and as a rule produces no symptoms. When the villi become long, however, they have been known to produce tickling and gagging. In some the lesion disappears spontaneously. In others treatment is of no avail.

Tonsillitis is a common infection particularly in childhood. It is caused by the ordinary pyogenic bacteria that are found in the mouth, especially the streptococci. They gain entrance by way of a break in the epithelium of the crypts and are prone to grow and multiply in the presence of ill-health, overwork or faulty lymphatic drainage. In acute tonsillitis symptoms consist of a sudden onset of pain and dryness in the throat, fever to 105°F, dysphagia, head-

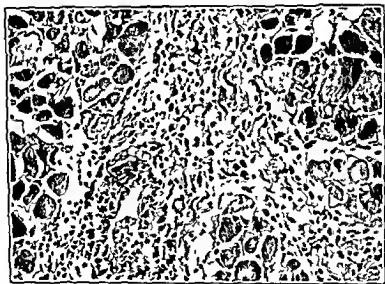


FIG. 216.—Ludwig's angina. There are edema of the intermuscular connective tissue and an infiltration with plasma cells, lymphocytes and neutrophils. $\times 100$.

ache, chilliness and general malaise. Pathologically, the tonsils (more commonly the palatine) are greatly enlarged, swollen, edematous, tender, red and are frequently covered with small flecks of exudate or with a grey pseudomembrane. The lymph nodes at the angle of the jaw are enlarged and tender. Since such tonsils are not removed surgically, one must resort to chance postmortem material for histologic studies. There are edema, congestion, and an infiltration with neutrophils, plasma cells and monocytes. With or without treatment symptoms usually regress in from three to five days and the patient completely recovers. Rarely, complications arise. These consist of otitis media, nephritis, arthritis, peritonsillar abscess (quinsy) or chronic tonsillitis. The latter encompasses a continuous low grade smoldering infection or repeated attacks of an acute infection that do not clear completely in the interim. There is al-

most always an associated inflammation of the adenoids. Together, these result in breathing through the mouth, impairment of speaking, hearing and taste, and repeated pulmonary infections. *Grossly*, the tonsils are usually enlarged but they may be contracted, scarred and ragged. *Histologically*, they disclose a hyperplasia of the follicles, a moderate increase of interfollicular plasma cells, monocytes, neutrophils and lymphocytes, an absence or a marked degree of fibrosis, and a deposition in the crypts of sloughed epithelial cells, bacteria and detritus.

Treatment consists of surgical removal. It must be pointed out, however, that the entire question of tonsillitis and tonsillectomy has been overemphasized and overexploited. Infections of these lymphoid structures are as frequent as is the common cold, but indications for their removal should not be merely the presence of tonsils, but should be limited to evidence of persistent chronic infection or of obstruction.

Peritonsillar abscess, also known as *quinsy*, is an acute inflammation of the peritonsillar connective tissue. The causative organism is usually the *streptococcus*. It gains entrance exogenously by way of the crypts, or more frequently by direct extension from an acute tonsillitis. Its peak incidence is in late winter or early spring, and it affects young adults almost exclusively. *Clinically*, there may or may not be a profound systemic reaction with chills, fever to 105°F and leukocytosis. There are pain in the throat with radiation to the ear, trismus, dysphagia and dyspnea. The *lesion*, initially at least, is confined to the supratonsillar fossa. There are fullness, swelling, redness, and edema not only of the fossa itself, but also of the uvula and soft palate. Characteristically, the tonsil is pushed down and medially, the uvula is shifted to the opposite side, and the isthmus faucium is encroached upon or obliterated. In a few days, the swelling becomes fluctuant and if untreated it ruptures into the mouth spontaneously within five or ten days. If seen early, *treatment* consists of antibiotic or chemotherapy. When an abscess forms this therapy is supplemented by a surgical incision parallel to the anterior pillar to release the pus. The tonsils are subsequently removed. Pending tonsillectomy, the *prognosis* should be guarded because recurrences are common. Some *complications* that occasionally arise are: edema of the glottis, strangulation from aspiration of pus, otitis media, cervical lymphadenitis, thrombophlebitis and erosion of a large vessel with even fatal hemorrhage.

Retropharyngeal abscess, as the name implies, is an abscess in the tissues between the pharynx and the vertebrae. Without further specification, it denotes an acute suppurative process in contrast to a tuberculous or cold abscess. The causative *organisms* are those usually found in the mouth or pharynx, and include streptococci, staphylococcus and less often pneumococci. They achieve *ingress* (1) from retropharyngeal lymph nodes that have become infected following nasopharyngitis, tonsillitis and similar local inflammations, (2) supervening trauma to the posterior wall of the pharynx, as for example, perforation during instrumentation or swallowing of a foreignbody, (3) as a result of malignant or simple ulceration of

the pharynx and (4) is an extension from otitis media, osteomyelitis of the cervical vertebra or an extradural abscess. Its greatest incidence is in children under three years of age, and it affects males twice as frequently as females. *Symptoms* are similar to those in peritonsillar abscess except that trismus is lacking and that there is in addition stiffness of the neck. Examination discloses a swelling of varying proportions in the retropharyngeal tissues that encroaches upon the pharyngeal space. *Treatment* consists of antibiotic or chemotherapy supplemented when necessary by internal or external surgical drainage. The *dangers* are extension to the mediastinum, septicemia, erosion of a vessel, and spontaneous rupture with resultant suffocation or pneumonia.

Specific Inflammation—Granulomatous lesions of the mouth and pharynx are less common than are non-specific inflammations. *Granuloma inguinale*, usually found in the inguinal regions and around the genitals, has been described in the buccal cavity as a result of auto-inoculation. *Lymphopathia venereum*, a venereal disease caused by a filtrable virus, has also been described in the mouth as a result of kissing, auto-inoculation or buccal coitus. The favorite site is the tongue, while enlargement of cervical lymph nodes is a constant finding. *Blastomycosis* and *histoplasmosis* are rare. *Boeck's sarcoid* affects the lymphoid tissue of the pharynx as a part of a generalized systemic disease. It has been considered in Chapter I. *Glanders*, while ordinarily attacking the nose, may extend to involve the pharynx, soft palate, larynx and even the trachea. It has been described in connection with the nasal cavity. Also *scleroma* and *leprosy* have been considered at length in Chapter III. Each of these may be located in any portion of the mouth or pharynx. Deserving of more than passing mention are syphilis, tuberculosis and actinomycosis.

Syphilis—The oral manifestations of *congenital syphilis* consist of (1) copper colored fissures and cracks that extend in a radiating fashion from the muco-cutaneous junctions of the lips. They are covered with a necrotic crust, contain the treponema pallidum and are known as *syphilitic rhagades*. When they heal they are replaced with permanent scars. (2) A deformity of the incisor teeth which become peg-shaped, with the broad portions at the gingival margin, and at the same time notched along their cutting borders. They are known as *Hutchinson's teeth*. *Acquired syphilis*, as elsewhere is divided into primary, secondary and tertiary stages. The *primary lesion* consists of a chancre and, although it may affect any portion of the oral or pharyngeal mucosa, it is usually found on the lips, tongue and tonsil. It is essentially similar to the genital chancre with the exception that it is less firm and slightly painful. It is a sharply circumscribed, indurated, raised sore that ulcerates centrally and spreads peripherally. In extra-oral lesions the denuded area is covered with brown to black, firm crusts, while in intra-oral sores, where there is abundant moisture, they are covered with a greyish white film. The regional lymph nodes are enlarged, firm and slightly tender. *Secondary lesions* are limited to mucous patches and are analogous to cutaneous papules and macules. They occur

most always an associated inflammation of the adenoids. Together, these result in breathing through the mouth, impairment of speaking, hearing and taste, and repeated pulmonary infections. *Grossly*, the tonsils are usually enlarged but they may be contracted, scarred and ragged. *Histologically*, they disclose a hyperplasia of the follicles, a moderate increase of interfollicular plasma cells, monocytes, neutrophils and lymphocytes, an absence or a marked degree of fibrosis, and a deposition in the crypts of sloughed epithelial cells, bacteria and detritus.

Treatment consists of surgical removal. It must be pointed out, however, that the entire question of tonsillitis and tonsillectomy has been overemphasized and overexploited. Infections of these lymphoid structures are as frequent as is the common cold, but indications for their removal should not be merely the presence of tonsils, but should be limited to evidence of persistent chronic infection or of obstruction.

Peritonsillar abscess, also known as *quinsy*, is an acute inflammation of the peritonsillar connective tissue. The causative organism is usually the *streptococcus*. It gains entrance exogenously by way of the crypts, or more frequently by direct extension from an acute tonsillitis. Its peak incidence is in late winter or early spring, and it affects young adults almost exclusively. *Clinically*, there may or may not be a profound systemic reaction with chills, fever to 105°F and leukocytosis. There are pain in the throat with radiation to the ear, trismus, dysphagia and dyspnea. The *lesion*, initially at least, is confined to the supratonsillar fossa. There are fullness, swelling, redness, and edema not only of the fossa itself, but also of the uvula and soft palate. Characteristically, the tonsil is pushed down and medially, the uvula is shifted to the opposite side, and the isthmus faucium is encroached upon or obliterated. In a few days, the swelling becomes fluctuant and if untreated it ruptures into the mouth spontaneously within five or ten days. If seen early, *treatment* consists of antibiotic or chemotherapy. When an abscess forms this therapy is supplemented by a surgical incision parallel to the anterior pillar to release the pus. The tonsils are subsequently removed. Pending tonsillectomy, the *prognosis* should be guarded because recurrences are common. Some *complications* that occasionally arise are: edema of the glottis, strangulation from aspiration of pus, otitis media, cervical lymphadenitis, thrombophlebitis and erosion of a large vessel with even fatal hemorrhage.

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In the *lips*, the lesions are found more often in the lower labium and, although they are located anywhere along the surface, they have a predilection for the mid portion and the angles. *Tonsillar* infections are rarely recognized clinically, but, histologically, tubercles are discovered in from 0.5 to 6.2 per cent of all tonsillectomies and in from 40 to 70 per cent of all cases with pulmonary tuberculosis. *Nasopharyngeal* lesions usually in the form of ulcers are most frequent in the posterior portion of the roof and upper part of the posterior wall, but they may also occur along the posterior margin of the eustachian tubes or the upper and posterior surface of the uvula and soft palate. Wherever the infections may be, the draining lymph nodes are usually involved in the tuberculous process. *Histologically*, the characteristic unit is the ordinary tubercle. As a rule there are no accompanying *symptoms*, but when the lesion is advanced there is severe, unremitting, and progressive pain.

A *diagnosis* is seldom possible from the gross appearance of the lesion alone. It is reasonably certain, however, if pulmonary tuberculosis is demonstrated, but it should always be confirmed by biopsy. *Treatment* consists of general anti-tuberculosis measures together with local hygienic care, and sometimes excision or destruction of the presenting lesion. The *prognosis* depends upon the severity of the pulmonary disease.

Actinomycosis—Human actinomycosis is caused by the actinomyces *bovis* and not by the fungi found on grain and grasses. The organism is a micro-aerophilic or anaerobic saprophyte that normally inhabits the mouth, and is particularly abundant in carious teeth and crypts of tonsils. From these locations, it serves as a focus of infection for lesions in the mouth, chest and abdomen. In the oral cavity, any break in the mucosa such as consequent to extraction of a tooth, chewing of splinters grass or grains, and simple nonspecific infection is usually the starting point of the infection. Three-quarters of all cases of actinomycosis in man are of the cervicofacial type. The disease affects males three times as frequently as it does females, is most common beyond the age of forty years, has no specific geographic distribution, and is encountered in people of all professions with, however, a slight preponderance among farmers.

The *lesion* starts as a small, round, solid, deep lump that is initially only slightly painful and tender. As it enlarges, the pain and tenderness increase, the mass becomes more superficial, undergoes central softening and necrosis, and in time, breaks through the surface discharging yellowish granular pus. The granules are colonies of actinomyces which can be readily identified in smears. Both the morphologic appearance of the organism and the histologic structure of the granuloma have been described in detail in Chapter I. The disease *spreads* by local extension rather than by the blood stream or lymphatics. In the mouth the most common *sites* of the lesions are the submaxillary tissues, cheeks, mandible, maxilla, gingivae, tongue, and tonsils. A definitive *diagnosis* can be made only upon finding the causative organism in smears of the pus or in histologic sections. The lesions are frequently confused

on the tongue, tonsils, pharynx and lips as circular erosions or ulcerating plaques of varying sizes. They are raised and exhibit a milky surface and an erythematous base with little induration. Mucous patches swarm with *treponema pallidum* and are, therefore, highly infectious. *Tertiary syphilitic lesions* are of the diffuse or more characteristically the gummatous type. The latter are usually found on the palate or the dorsum of the tongue, first as submucosal nodules and then, with liquefaction and sloughing of their centers, as deep ulcers. The ulcerations are serious for they eventuate in large defects or perforations, particularly of the hard and soft palates. They heal by fibrosis and thus, frequently, form adhesions between the soft palate and the pharynx. Aside from lesions of the soft tissues of the mouth tertiary syphilis may exist in the form of periostitis, periodontitis and osteomyelitis. *Histologically*, syphilitic inflammations in the mouth are the same as those elsewhere, and these have been considered in detail in Chapter I. In the initial stages the *diagnosis* may be difficult, for in dark field examination *treponema pallidum* is easily confused with a saprophytic oral spirochaete—the *treponema microdentium*. One must, therefore, rely upon a history of exposure and, several weeks later, upon a positive serologic test for syphilis. Tertiary lesions are frequently confused with carcinoma and the diagnosis is, therefore, inadvertently made from a biopsy. *Treatment* consists of anti-syphilitic measures which have already been outlined in Chapter I.

Tuberculosis.—Tuberculosis of the mouth and pharynx accounts for from 0.35 to 3.65 per cent of all tuberculous infections. It is seen somewhat more frequently in men than in women, and it is most prevalent in the third and fourth decades of life. Most of the cases are *secondary* to advanced pulmonary tuberculosis and only a minority result from an exogenous source. The *pathogenesis* has been a subject of considerable controversy, but most observers agree that the majority of infections are sputogenic, that only a few are hematogenous, and that the lymphogenous route of spread is quite unlikely. Although tuberculosis of the mouth and pharynx occurs in as many as 75 per cent of the cases of pulmonary tuberculosis coming to necropsy, the number of cases in living patients with positive acid-fast bacilli in the sputum is considerably less. This immunity is ascribed to the relatively thick mucosa, to the movements of the tongue, to the mechanical cleansing of the saliva, food and air, and to the bacteriostatic action of the saliva. A predisposing cause of the infection is some break in the mucosa as a result of either a preliminary non-specific infection or trauma, such as incurred from a ragged tooth.

Over one-half of the *lesions* are found on the *tongue*, while the rest are distributed among the lips, tonsils and nasopharynx. Lingual infections are usually present along the lateral margins or the tip, but occasionally they affect the dorsum or other areas. In over 90 per cent of the cases, they exist as ovoid or irregular undermined, ragged ulcers exhibiting yellowish grey necrotic bases and often small tubercles about the periphery. In the remainder, they are present as fissures, granulomas, tuberculomas or as a more diffuse glossitis.

of ectoderm that have been entrapped in the soft tissues of the submental region. It may become manifest in infancy or not until adolescence is a smooth, round or oblong, sharply delineated non-adherent painless swelling in the floor of the mouth. It bulges either externally or sublingually, is usually midline in position, but, when it becomes larger, it may extend to one side or the other. As a rule it produces no symptoms, although it may encroach upon the buccal or pharyngeal space resulting in difficulty in chewing, swallowing and breathing. *Anatomically*, it is located beneath the skin

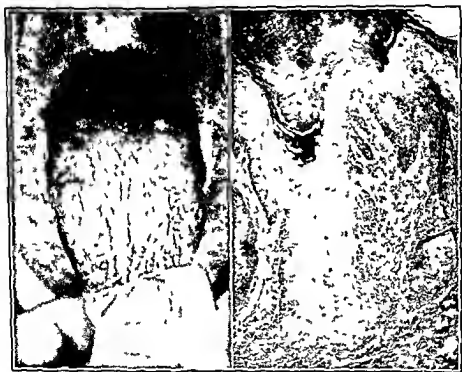


FIG 218

FIG 219

FIG 218—Leukoplakia of the tongue. The irregular area along the right lateral border posteriorly is early carcinoma.

FIG 219—Same case illustrated in figure 218. There are marked hyperkeratosis, proliferation of the rete pegs, and an infiltration of the papillae with plasma cells and lymphocytes. $\times 25$.

or between the geniohyoid muscles. It varies in size but the average diameter at the time of removal is about 5 cm. The mass is soft or dough-like and on section presents central, semisolid or fluid greasy material sometimes admixed with hair and a surrounding thin capsule (Fig 217). The latter consists of an inner lining of stratified squamous epithelium and an outer layer of dense fibrous tissue. It may contain hair follicles and sebaceous glands. When the cyst becomes infected it may be mistaken for Ludwig's angina. Otherwise, it should be differentiated from aberrant thyroid gland, thyroglossal cyst and branchial cyst. The treatment is complete excision. The prognosis is excellent.

with tuberculosis, syphilis and carcinoma. *Treatment* consists of surgical excision when the mass is small and not yet necrotic, of incision when there is suppuration, of administration of potassium iodide and more recently of antibiotics, and of irradiation therapy. If treated correctly and early, the *prognosis* of cervico-facial actinomycosis is good.

Tumors.—Neoplasms of the mouth, pharynx and their various organs are as disparate as the tissues that compose them. On a histogenetic basis they may be grouped as follows: from epithelium there arises an aberrant thyroid, thyroglossal duct and cyst, epidermoid cyst, mucous cyst, leukoplakia, papilloma, mixed tumor, and carcinoma; from connective tissue a fibroma, myxoma, and fibrosarcoma; from fat tissue a lipoma and liposarcoma; from vessels a lymphangioma and hemangioma; from lymphoid tissue or reticulum cells any of

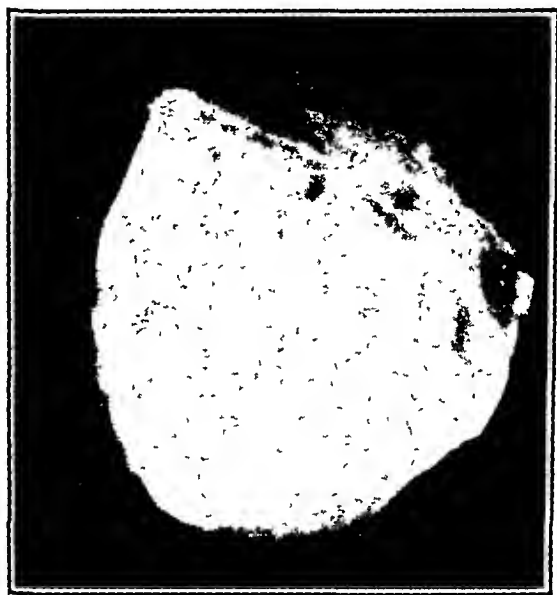


FIG. 217.—Epidermoid cyst from the floor of the mouth, filled with thick, grey, greasy material. Natural size.

the tumors that are found in these structures elsewhere in the body (see Chapter XVI); from nerves or their derivatives neurofibroma and melanoblastoma; from muscle a leiomyoma, rhabdomyoma and rhabdomyosarcoma; from teeth or their various components an epulis and other tumors that may be called odontogenic; from osseous tissue any of the neoplasms that are described in the section on bones; from fat, connective tissue or histiocytes (reticulum cells) a xanthoma, and from distant organs metastatic tumors. Some of these growths have already been described; others will be considered in ensuing chapters; most are self-explanatory and since many of them are rare they will not be discussed further; only a few are frequent enough and important enough to merit elucidation.

Epidermoid Cyst.—This growth has already been mentioned under midline epithelial inclusions in the section on the skin. It is a developmental anomaly that results from cystic dilatation of pieces

of ectoderm that have been entrapped in the soft tissues of the submental region. It may become *manifest* in infancy or not until adolescence as a smooth, round or oblong, sharply delineated non-adherent painless swelling in the floor of the mouth. It bulges either externally or sublingually, is usually midline in position, but, when it becomes larger, it may extend to one side or the other. As a rule it produces no *symptoms*, although it may encroach upon the buccal or pharyngeal space resulting in difficulty in chewing swallowing and breathing. Anatomically, it is located beneath the skin



FIG 218

FIG 219

FIG 218—Leukoplakia of the tongue. The irregular area along the right lateral border posteriorly is early carcinoma.

FIG 219—Same case illustrated in figure 218. There are marked hyperkeratosis, proliferation of the rete pegs and an infiltration of the papillae with plasma cells and lymphocytes. $\times 25$.

or between the geniohyoid muscles. It varies in size but the average diameter at the time of removal is about 5 cm. The mass is soft or dough-like and on section presents central, semisolid or fluid greasy material sometimes admixed with hair and a surrounding thin capsule (Fig 217). The latter consists of a inner lining of stratified squamous epithelium and an outer layer of dense fibrous tissue. It may contain hair follicles and sebaceous glands. When the cyst becomes infected it may be mistaken for Ludwig's angina. Otherwise, it should be differentiated from aberrant thyroid gland, thyroglossal cyst and branchial cyst. The treatment is complete excision. The prognosis is excellent.

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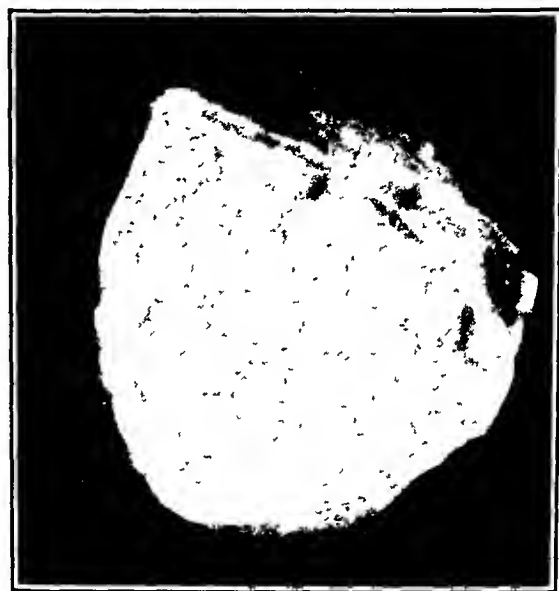


FIG. 217.—Epidermoid cyst from the floor of the mouth, filled with thick, grey, greasy material. Natural size.

the tumors that are found in these structures elsewhere in the body (see Chapter XVI); from nerves or their derivatives neurofibroma and melanoblastoma; from muscle a leiomyoma, rhabdomyoma and rhabdomyosarcoma; from teeth or their various components an epulis and other tumors that may be called odontogenic; from osseous tissue any of the neoplasms that are described in the section on bones; from fat, connective tissue or histiocytes (reticulum cells) a xanthoma, and from distant organs metastatic tumors. Some of these growths have already been described; others will be considered in ensuing chapters; most are self-explanatory and since many of them are rare they will not be discussed further; only a few are frequent enough and important enough to merit elucidation.

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causative factors. In some cases, the lesion disappears but in others, it persists despite all therapeutic measures.

Mixed Tumors—Mixed tumors of the salivary gland type are not uncommon in the mouth. They affect both sexes with approximately equal frequency, usually occur in the sixth decade, and are of a few weeks to many years duration. About one-third of the patients are symptomless. The rest, depending upon the size and location of the tumor, may complain of irritation, pain radiating to the ear or teeth, fullness in the throat, dysphagia, cough, nasal obstruction and deafness. The lesions occur on the hard and soft palate, buccal mucosa, base of the tongue, tonsillar pillars, alveolar ridge, upper lip and rarely, the lower lip. They are single, nodular, sharply circumscribed, round or oval, non-tender, freely movable, firm or less often semisolid, submucosal tumors that average about 1 cm in diameter (Fig 220). The surface epithelium is usually intact, but, rarely, it may be ulcerated. Histologically, they are

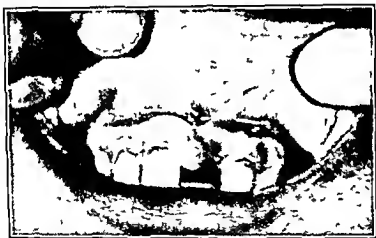


FIG 221—Epulis

composed of varying proportions of epithelial cells and mesodermal elements and are, therefore, similar to mixed tumors of the salivary glands. Although they have been considered to arise from misplaced salivary glands and from branchial cleft remains, one need not look further than the submucosal glands to explain their genesis. A diagnosis is made from the appearance and location of the tumor coupled with a history of long duration all in a patient in the sixth decade of life. It may be confused with a *gumma* and with *torus palatinus* (osteoma of the hard palate that protrudes into the mouth). Treatment is surgical excision. If completely extirpated it does not recur. If untreated the tumor is locally invasive and destructive, and sometimes it becomes malignant, metastasizing to the upper cervical lymph nodes and distant organs. Death occurs from the secondary lesions.

Epulis—An epulis is a benign tumor that grows on the gingiva. It is found three times as frequently in females as it is in males, involves the outer rather than the inner surface of the gums, and

Leukoplakia.—Leukoplakia is included in this section merely for convenience, because it is a hyperkeratosis of the epithelium and not a true tumor. It affects ten men to every woman, is rare before the age of fifty years and is usually asymptomatic. When cracks or fissures become infected, however, there may be associated pain and when the lesion is extensive it may interfere with motility of the cheeks, lips and tongue. Although the *cause* of leukoplakia is not known, the following have been considered to play an etiologic rôle: individual susceptibility, hormones, vitamin A deficiency, syphilis, trauma from ragged teeth, faulty occlusion or ill-fitting dentures, and irritation from chemicals, heat, poor oral hygiene, tobacco and highly seasoned food. The most frequent *sites* of in-



FIG. 220 —Mixed tumor of the soft palate. (Courtesy Dr. Warren B. Davis)

volvement are the tongue, cheeks, lips, palate and gingiva. The initial *lesion* consists of a red, granular, sharply defined, somewhat sensitive area which is replaced in time with a bluish white or grey plaque that appears to be plastered on the surface. Later, the color changes to pearly white; the surface becomes wrinkled, fissured or eroded, and the base becomes indurated and leathery (Fig. 218). *Histologically*, the first change is an infiltration of the superficial part of the corium with lymphocytic cells. This is followed by a keratosis and increased thickness of the superficial cells, by a hypertrophy and hyperplasia of the prickle cell layer, by an enlargement of the rete pegs, and by an intensification of the lymphocytic infiltration of the papillae of the corium (Fig. 219). A *diagnosis* is made from the gross appearance of the lesion. If the plaque is eroded, a biopsy must be resorted to because such areas are prone to *cancerous* transformation. *Treatment* consists of the removal of all possible

causative factors In some cases, the lesion disappears but in others, it persists despite all therapeutic measures

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FIG 221—Epulis

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affects the upper jaw more often than the lower. It arises from the periostium or the periodontal membrane and presents as a painless, symptomless, inter-dental growth that has a tendency to separate the teeth. It is pedunculated or sessile, well-circumscribed, smooth, non-ulcerated, livid or pink, soft or firm, and measures from a few millimeters to 6 cm. or more in diameter (Fig. 221). *Histologically*, there are two types. One is composed entirely of cellular or acellular fibrous tissue in which there may or may not be a superficial leukocytic infiltration, and the other is composed of a fibrous tissue stroma throughout which there are numerous giant

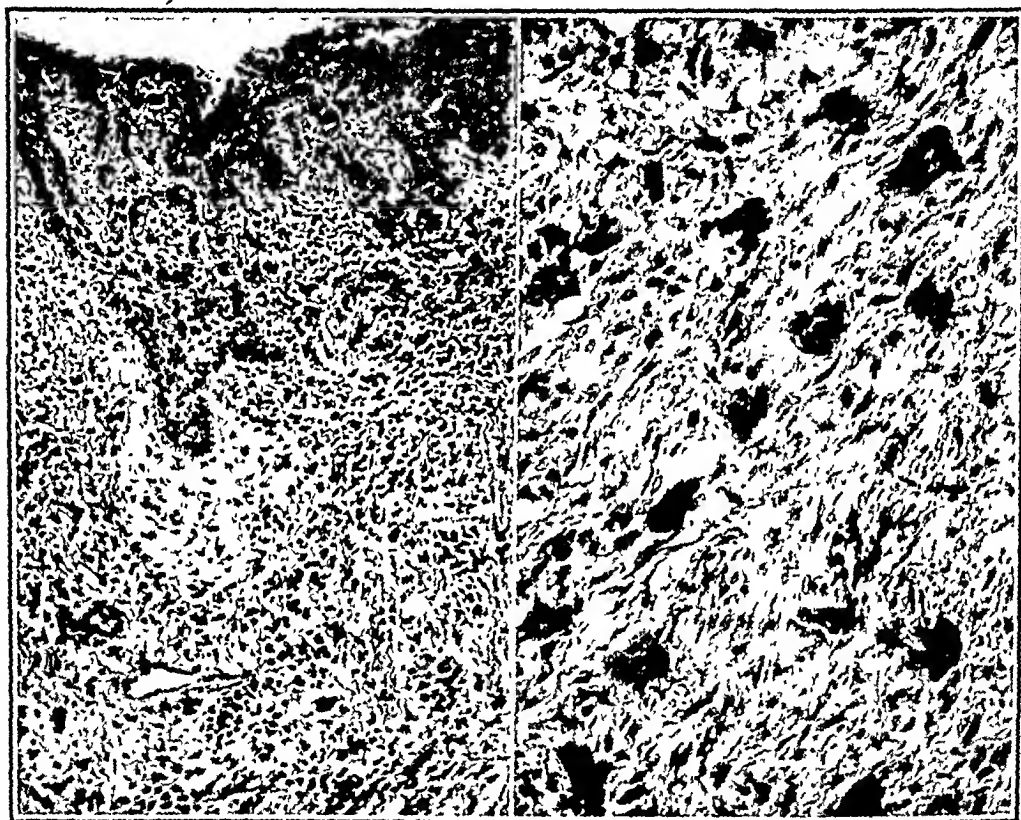


FIG. 222

FIG. 223.

FIG. 222.—Epulis from case shown in figure 221. It is composed of a loose connective tissue stroma that is densely infiltrated with plasma cells and lymphocytes. $\times 50$.

FIG. 223.—Epulis composed of a dense fibrous tissue stroma in which there are numerous giant cells of the foreign body type. $\times 100$.

cells of the foreign body type (Figs. 222 and 223). *Treatment* is complete surgical excision, and this sometimes necessitates extraction of the tooth on each side of the tumor. If entirely extirpated, the lesion does not recur.

Odontogenic Tumors.—The teeth are complex structures and tumors arising from dental or potential dental tissues must, therefore, be protean in composition. They may be divided into the following four groups: (1) *cysts* consisting of two main types—simple without tooth formation and dentigerous which contains a tooth, (2) *epithelial growths*—the adamantoblastomas which are soft and the enamelomas which are calcified, (3) *mesenchymal neoplasms*—if soft they

containing collections of submucosal lymphoid tissue, such as the base of the tongue and the nasopharynx, may be the site of a specific type of epithelial tumor—the lymphoepithelioma which grossly is quite distinctive. It has a tendency to grow submucosally, to penetrate the underlying tissue, to remain small locally and to metastasize early. Such a tumor is easily missed even upon careful inspection for it may be only a few millimeters in diameter, is not raised appreciably above the surface and may show only a superficial roughening of the mucosa.

Histologically, the tumors arise either in the basal cells of the mucosa or in the submucosal glands. If mixed tumors are excluded

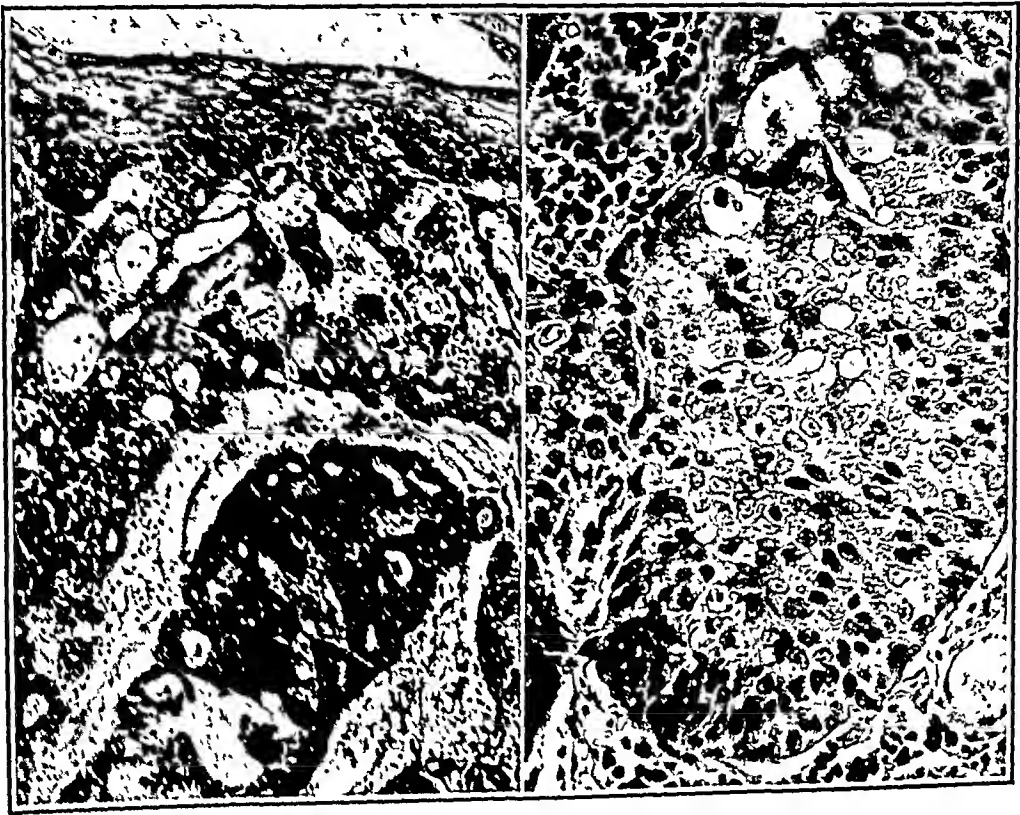


FIG. 227.

FIG. 228

FIG. 227.--Basal cell carcinoma of the tongue. $\times 50$

FIG. 228. --Epidermoid carcinoma of the tongue without pearl formation $\times 100$

form an odontogenic fibroma, if calcified and contain dentine they form a dentinoma, and if calcified and contain cementum they form a cementoma, (4) *mixed tumors*. These consist of epithelial and mesodermal derivatives with or without recognizable teeth or portions of teeth in varying stages of development. Of all the foregoing lesions the adamantinoblastoma has perhaps received most attention.

The adamantinoblastoma has been described under many other names the most popular of which is adamantinoma. The latter is a misnomer for the term means a growth containing enamel and the tumor, although it consists of adamantinoblasts, never forms adamantine. The neoplasm affects males as often as females, has been described at all ages from birth to seventy-six years with an average of thirty years, and occurs in the mandible in 84 per cent of the cases.



FIG. 224.—Adamantinoblastoma showing central cells undergoing cystic degeneration, a peripheral layer of cylindrical cells and a stroma of dense fibrous tissue. $\times 100$

The only *symptoms* are swelling and pain. The average duration of the lesion in the recorded cases has been 8.5 years, but in any single case the duration may be as many as fifty years. A frequent history is that the growth has been operated upon previously without success. A roentgenogram discloses a unilocular or multilocular tumor that destroys a portion or all of the bone. *Grossly*, the growth is solid or cystic but it has no pathognomonic features.

Histologically, it consists of cords or nests of epithelial cells embedded in a scanty or almost absent connective tissue stroma. The centers of the masses are composed of stellate cells that frequently have a tendency to undergo degeneration, liquefaction and cystic formation (Fig. 224). The periphery is covered with a single layer of cuboidal or cylindrical cells. They are arranged at right angles to the surface and externally rest upon a basement membrane. The cytoplasm is scanty or moderate in amount and lightly stained,

and the nuclei are round or oval and uniform. A few of the tumors bear some resemblance to ordinary squamous cell carcinomas and others are similar to both the solid and cystic basal cell carcinomas. The *diagnosis* is made from the location of the lesion, a chronic course, a typical roentgenographic appearance and finally from the histologic structure. *Treatment* is complete surgical excision. *Recurrences* are frequent, but a malignant transformation with metastasis is extremely rare. Because of its persistence, however, the *prognosis* is not favorable.

Carcinoma.—Cancer of the mouth and pharynx is a common and serious disease. Its *causes*, as in other portions of the body, are not definitely known, although there are certain factors and lesions peculiar to this region that have a bearing upon their development. Most of the predisposing agents are in the form of chronic irritants and include the following: avitaminosis B, tobacco (as a result of both a thermal and a chemical action), ragged teeth, ill-fitting dentures, improper oral hygiene, treponema pallidum, and actinic rays. Obviously, all of these do not operate in all areas, for actinic rays have no effect beyond the lips, the teeth do not influence nasopharyngeal carcinoma, tobacco has little effect on the floor of the mouth and so forth. The *lesions* that predispose to or that *precede carcinoma* are characterized by their chronicity, and include such conditions as chronic non-specific ulcers, leukoplakia, keratosis, atrophy, dryness, fissures and scars. Eighty to 98 per cent of all cases of carcinoma of the mouth and pharynx are found in males; the average age is fifty-five to sixty-two years except for nasopharyngeal growths where it is forty-five years, and, in the United States, the white race is affected more often than the colored. *Symptoms* will, of course, differ somewhat with the site of the lesion. In cancer of the lip, a frequent story is the presence of a cold sore, fever blister, crack, wart or ulcer that breaks down, heals and reappears. In lesions of the oral cavity proper, there may be noticed a tumor or an ulcer which, however, produces no pain or discomfort until secondarily infected. If the growth is on the gingivae, it may by extension into the bone cause a loosening of the teeth, if in the floor of the mouth the pain often radiates to the ear, if extensive and in the tongue, tonsil or palate it will infiltrate the muscles of deglutition and produce dysphagia and trismus, and if in the nasopharynx, it may cause unilateral deafness, nasal obstruction, headache and (because of extension into the cranium) it may eventuate in a destruction of the sixth, third, fourth, fifth, seventh and second cranial nerves. In over one-half of the cases of carcinoma of the nasopharynx and base of the tongue, and in varying proportions of growths in other areas, the first indication of trouble is a mass in the neck or beneath the jaw. So important is this sign that in an adult an enlarged, firm, non-tender, cervical lymph node should, therefore, be regarded as metastatic carcinoma until proved otherwise.

Although the neoplasms can occur anywhere in the mouth or pharynx, they have *sites of predilection*. In cancer of the *lips*, the lower is involved in about 90 per cent of cases, the upper in 8 per cent

and the commissures in 2 per cent (Fig 225) In the *gingivae*, the lesion occurs most often opposite the third molar and then the bicuspids and canine teeth In the *floor* of the *mouth*, the most commonly affected area is the anterior portion to one side of the midline and near the openings of the submaxillary ducts In the *tongue*, two-thirds of the lesions occur along the edge and middle third, whereas the bulk of the rest arise in the base (Fig 226) In the *palate*, three-fourths of the cancers are located in the soft portion and most of these are found along the free border In the *tonsil*, the point of origin is difficult to determine because the growths on admission usually cover the entire surface In the *pharynx*, the approximate order of frequency is the superior portion of the posterior wall, around the orifice of the eustachian tubes, hypopharynx,



FIG 225

FIG 226

FIG 225—Ulcerating carcinoma of the upper lip

FIG 226—Carcinoma of the tongue

upper surface of the soft palate and the posterior portion of the nasal septum

Grossly, the tumors vary somewhat according to their age, location, histologic composition and amount of secondary infection The initial lesion in the lip may appear as a bleb, a nodule or an ulcer The latter is superficial, small, irregular, flat, and is covered with a crust which upon removal leaves a raw bleeding surface Later the area becomes raised, firm, coarsely granular, ulcerates deeper, has a grey necrotic floor and elevated somewhat undermined edges, and infiltrates the adjacent tissues so that to palpation the lesion is always larger than it is to inspection Less frequently, labial growths are elevated, papillary and fungating with a pedunculated base and only a superficially ulcerated surface If the growths are not too large, there may be noted leukoplakia of the surrounding mucosa Lesions in the oral cavity proper and those in the pharynx are likewise of these two types They differ only in that their surfaces lack the scaliness that the early labial growths possess, due to the ever abundant moisture In addition, the areas

containing collections of submucosal lymphoid tissue, such as the base of the tongue and the nasopharynx, may be the site of a specific type of epithelial tumor—the lymphoepithelioma which grossly is quite distinctive. It has a tendency to grow submucosally, to penetrate the underlying tissue, to remain small locally and to metastasize early. Such a tumor is easily missed even upon careful inspection for it may be only a few millimeters in diameter, is not raised appreciably above the surface and may show only a superficial roughening of the mucosa.

Histologically, the tumors arise either in the basal cells of the mucosa or in the submucosal glands. If mixed tumors are excluded

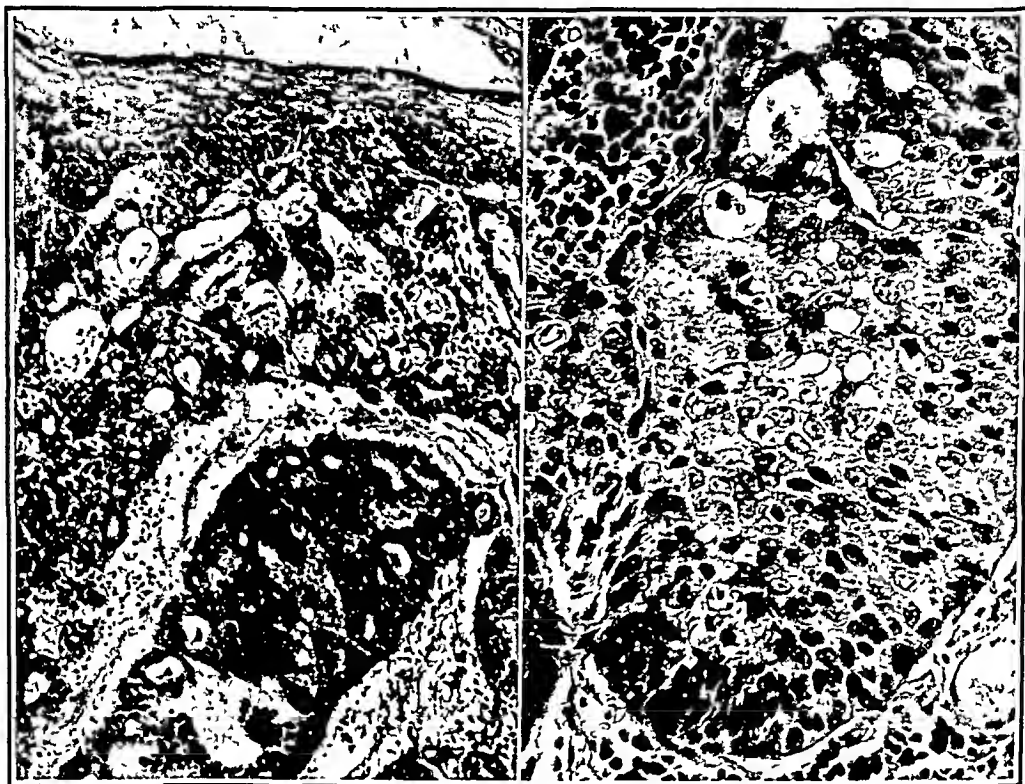


FIG 227

FIG 228

FIG. 227.—Basal cell carcinoma of the tongue. $\times 50$.

FIG. 228.—Epidermoid carcinoma of the tongue without pearl formation. $\times 100$.

the latter are so rare that for all practical purposes they may be disregarded. Those that arise in the basal cells of the mucosa usually produce a squamous cell carcinoma but on rare occasions they may be responsible for a *basal cell growth*. Although the latter is more frequent on the lips it may occur within the oral cavity proper (Fig. 227). As in other locations the covering mucosa is at first intact but streaming from the basal cells into the underlying tissue there are nests, strands and clusters of neoplastic cells. These have a moderate to scanty amount of light pink to basophilic cytoplasm and round or oval evenly stained nuclei. Frequently the central cells degenerate, liquefy and are replaced with cysts that are filled with stringy, pink or basophilic material. The supporting tissue is edematous, quite vascular and infiltrated with plasma cells.

lymphocytes and neutrophils. This tumor is indistinguishable from some of the mixed tumors of the submucosal glands and when an origin in the covering mucosa cannot be demonstrated its histogenesis is uncertain. Far more frequent is the *squamous cell carcinoma*. As in the skin and elsewhere this type of growth may appear (1) as an ordinary *well differentiated* cancer with abundant keratinization and numerous pearls, (2) as an epidermoid carcinoma without pearl formation or (3) as an anaplastic tumor. The first of these needs little additional comment. If sections are secured at the correct level, cords and sheets of polyhedral prickle cells arising from the mucosa are seen to infiltrate the underlying tissues. As always they possess an abundant amount of eosinophilic cytoplasm and round, oval or irregular hyperchromatic nuclei that are frequently in a state of mitosis. The central cells tend to be grouped in closely packed concentric lamina about a completely keratinized group of epithelial cells to form the well-known pearls.

The second type, namely, *epidermoid carcinoma without keratinization* or pearl formation is less common. It consists of sharply defined nests, sheets or strands of moderately sized round or oval cells with indistinct boundaries (Fig 228). The cytoplasm is relatively scant and lightly basophilic, and the nuclei are round or oval and evenly stained or hyperchromatic. Mitoses are numerous. The third type, namely, *anaplastic carcinoma* is also less frequent than the well-differentiated variety. This group is quite variform. At one extreme there is more or less a diffuse sheet of closely connected or disunited polyhedral cells that can still be recognized as prickle cells (Fig 229). They are, however, extremely irregular in configuration. Their borders are sharp, their cytoplasm is abundant or scanty and eosinophilic or lightly basophilic, and their nuclei are round, oval or bizarre, hyperchromatic and often in a state of mitosis. At the other extreme the anaplastic cancers are represented by completely disunited round or spindle cells that resemble a sarcoma (Fig 230). The cytoplasm is scanty, eosinophilic and peripherally indistinct, and the nuclei are round or spindle shaped and evenly but deeply basophilic. In all squamous cell carcinomas, the supporting stroma varies, is scanty or abundant, dense or edematous, and contains varying numbers of plasma cells, lymphocytes, neutrophils and other leukocytes.

As already stated the epithelium overlying collections of lymphoid tissue may give rise to a tumor called *lymphoepithelioma* or *Schminke tumor*. The literature on this group of carcinomas is quite confused. In ones that give rise to these growths, the mucosa is more of a transitional cell type than of a squamous variety. The question then arises, should all these neoplasms be labelled transitional cell carcinoma or should this caption be reserved for lesions composed only of groups of transitional cells and should those in which there is an intermingling of lymphocytes be called lympho-epithelioma? The query is, however, purely academic. In either case there are sharply circumscribed or ill-defined nests and sheets of pale staining epithelial cells that unhesitatingly infiltrate the submucosa and deeper tissue (Fig 231). They originate in the covering mucosa, but un-

containing collections of submucosal lymphoid tissue, such as the base of the tongue and the nasopharynx, may be the site of a specific type of epithelial tumor—the lymphoepithelioma which grossly is quite distinctive. It has a tendency to grow submucosally, to penetrate the underlying tissue, to remain small locally and to metastasize early. Such a tumor is easily missed even upon careful inspection for it may be only a few millimeters in diameter, is not raised appreciably above the surface and may show only a superficial roughening of the mucosa.

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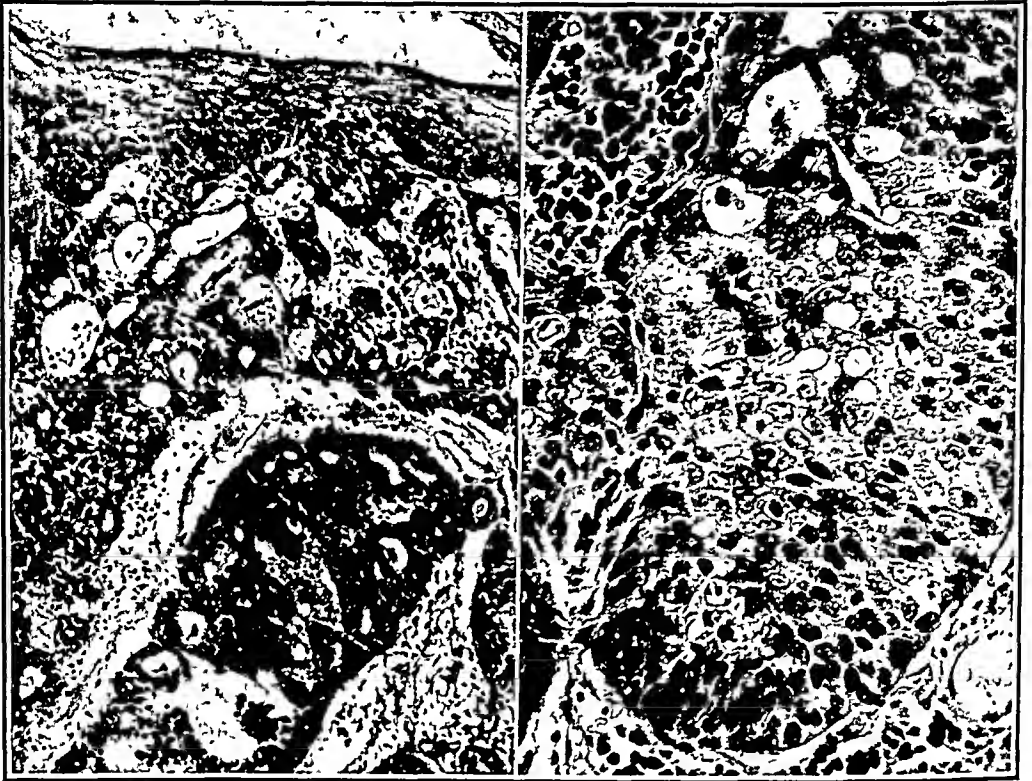


FIG 227

FIG 228

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like in other cancers the latter is frequently left intact. The cells are uniform and of moderate sizes. They have a moderate, abundant or scanty amount of light staining cytoplasm and round, oval or somewhat irregular vesicular nuclei. The number of mitoses varies. As a rule, there is an intimate intermingling with lymphocytes, but sometimes the latter are in complete abeyance.

The *spread* of carcinoma of the mouth and pharynx is by local extension, by lymphatic vessels and rarely by the blood stream. By contiguity the cancer invades and destroys all adjacent tissues. In

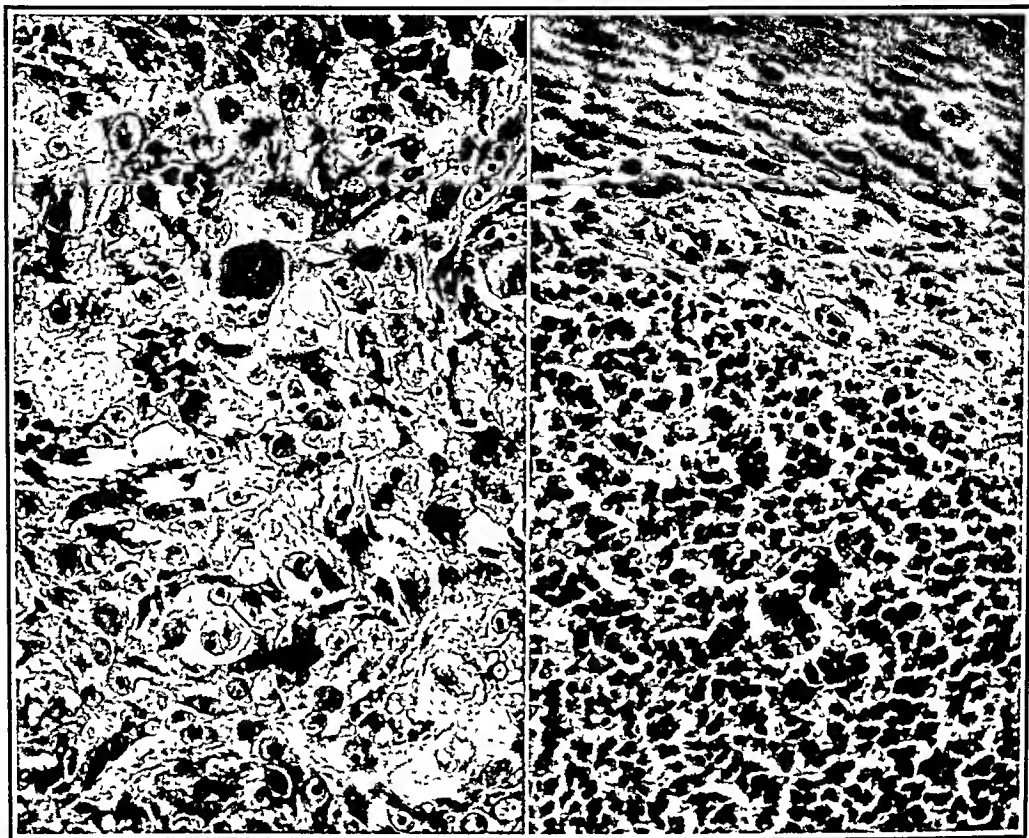


FIG. 229.

FIG. 230

FIG. 229.—Anaplastic carcinoma of the tongue of a prickle cell variety. x 100.

FIG. 230.—Anaplastic round cell carcinoma of the tongue. x 100.

the lip, it ulcerates and eventually destroys most of the labium. In the tongue and floor of the mouth, it infiltrates the lingual muscles and makes the tongue immobile. From the tonsils and soft palate, it extends into the masseter muscles and produces trismus. In the nasopharynx, it occludes the eustachian tube and by way of the foramen lacerum, it extends into the cranium where it destroys most of the first seven cranial nerves. The lymph nodes that are affected by secondary growths vary according to the location of the primary neoplasm. Thus from the upper lip, metastasis occurs to the preauricular and parotid nodes; from the lower lip to the submaxillary and less commonly the submental nodes; from the gums and floor of the mouth to the submaxillary and deep cervical nodes, and from

the tongue, tonsil, palate and nasopharynx to the upper deep cervical nodes. Metastasis by the blood stream is, as already stated, rare and when it does occur it is usually a terminal event. It is present most frequently in cancer of the tongue and pharynx.

A definitive *diagnosis* of carcinoma, as elsewhere, must rest with a biopsy. Tumors of the palate must be differentiated from torus palatinus, and those of the dorsum of the tongue from median rhomboid glossitis. In these and other locations, a differential diagnosis also includes leukoplakia, tuberculosis, gumma, papilloma and actinomycosis. *Treatment* of oral and pharyngeal carcinoma is not standardized. Lesions of the lips and the smaller ones of the gums can be cured by surgical excision or irradiation, but those in other locations should be treated by irradiation alone. Lymph node metastases are treated by surgical dissection, irradiation or by

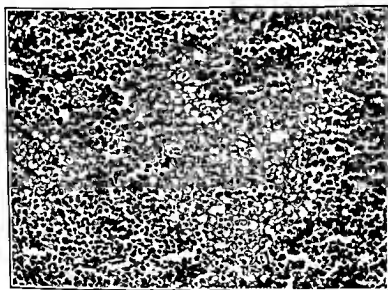


FIG. 231.—Lymphoepithelioma of the pharynx showing sheets of epithelial cells intermingled with lymphocytes. $\times 100$

a combination of these two. *Complications* that may arise consequent to roentgen or radium therapy are irradiation sickness, pain, radionecrosis, hemorrhage, dental disturbances, osteomyelitis, edema of the larynx and, from aspiration of septic material, pneumonia and pulmonary abscess. The *prognosis* varies according to the age and sex of the patient and according to the localization, size and site of the lesion. The best age group is the sixth decade and the favored sex is the female. As would be expected, the outlook is better in those cases where the lesion is confined to the original site than in those with metastases, and it is also better in smaller growths than in larger ones. With regards the organs involved the five year cure rate should be approximately 100 per cent in cancer of the lip, 25 per cent in carcinoma of the gums, floor of the mouth, tongue, palate, and nasopharynx, and about 18 per cent in epithelial growths of the tonsil.

Mechanical Disturbances.—These may be briefly considered under (1) trauma to the teeth (2) fractures of the jaws and (3) traumatic gingivostomatitis.

Trauma to the *teeth* may result from a direct blow or from a blow transmitted through the jaw. If it is mild it produces concussion which results in temporary soreness. Rupture of dental vessels is accompanied by hemorrhage that later imparts a grey or black color to the tooth. It may be associated with necrosis of the pulp. If trauma is more severe it produces luxation or displacement of a portion or an entire tooth. This is often associated with fracture of the alveolar bone and may eventuate in hemorrhage, necrosis and suppuration of the pulp. If trauma is still greater, it results in fracture of the tooth. If the break is external to the pulp a covering layer of secondary dentine may form and the tooth heals, but if the fracture is through the pulp it may cause necrosis of the pulp and infection.

Fractures of the *jaws* are also the result of direct or indirect trauma. They may be simple—without injury to the surrounding tissues, compound—when the adjacent tissue is lacerated, single—one fracture line, multiple—more than one fracture line, comminuted—when the bone is broken into many pieces, depressed—when the bone is driven into a cavity, and impacted—when the broken ends are pegged into each other. Fracture of the jaw may be accompanied by syncope, shock, and obstruction to the airway by broken dentures, teeth, bones, blood clots or a falling back of the tongue. There is usually deformity due to displacement of fragments and edema, discoloration of tissue due to hemorrhage, and infection due to entrance of bacteria. The extent and type of fracture and the results of treatment are always determinable in roentgenograms.

Traumatic gingivostomatitis is an inflammation and ulceration of the gums and buccal mucosa consequent to mechanical injuries. Trauma to the lips and cheeks is usually caused by perforations from teeth and is incurred in falls, fights, accidents or by biting. Injury and irritation to the gums is *produced by* diversified agents, as for example, improper brushing, faulty eating habits particularly when teeth are missing, chewing on hard objects, sharp edges of fillings, carious teeth, ill-fitting dentures, and numerous foreign bodies such as calcareous deposits, pieces of tooth picks, tooth brush bristles, chicken and fish bones, and various dental and orthodontic appliances. In addition to some of the aforementioned agents, injuries to buccal and pharyngeal mucosa may also result from hot foods and beverages, steam, tobacco, snuff, alcohol, suicidal drugs, chromic acid, phenol, creosote, silver nitrate and other chemicals.

SALIVARY GLANDS

EMBRYOLOGY

The salivary glands arise from the buccal epithelium as buds which soon arborize into solid ducts. The terminal portions of these become bulbous and ultimately differentiate into secretory acini,

while the proximal portions are hollowed out and persist as the main ducts. The surrounding mesenchyme forms the capsule and sends septa into the gland proper dividing it into lobules. Each parotid gland appears at the tenth week of embryonic life near the angle of the jaw lateral to the groove that divides the cheek from the gum. Each submaxillary gland arises a few days later as a ridge in the groove between the lower jaw to one side of the midline. Each sublingual gland consists of a major gland along with about ten smaller glands, and all originate from separate epithelial buds that appear in the groove between the tongue and lower jaw. The labial, buccal and palatine glands arise about the third month of embryonic life.

ANATOMY

Throughout the submucosa of the oral cavity there are numerous small salivary glands that are named according to their location. In addition, there are three pairs of larger glands that are called the parotid, submaxillary and sublingual. Each *parotid gland* weighs approximately 25 gm and is roughly pyramidal in shape. It is enveloped by a stout capsule that is continuous with the deep cervical fascia. The upper surface of the gland is concave and encircles the external acoustic meatus and the posterior mandibular joint. The inner surface covers the masseter muscle, mandibular joint and the facial nerve above, while inferiorly it overlies the mastoid process, sternocleidomastoid muscle, styloid process, and the external carotid artery. Its duct, also called *Stensen's duct*, emerges from the union of numerous small ducts within the gland. It is 5 cm long. It crosses the surface of the masseter muscle, and at its anterior border it makes a right angle turn and pierces the oral mucosa of the vestibule opposite the upper second molar tooth. The *arterial* supply comes from the external carotid, the *lymphatics* drain into the superficial and deep cervical lymph nodes, and the *neries* arise in the facial auriculotemporal and greater auricular nerves and the sympathetic plexus that covers the external carotid artery. Each *submaxillary gland* measures about 2.5 cm in greatest diameter. It is located in the floor of the mouth and consists of a larger superficial portion and a smaller deeper portion that are partly separated from each other by the posterior border of the mylohyoid muscle. The *submaxillary duct* (also called Wharton's duct) is 5 cm long. It courses between the mylohyoid and hyoglossus and beyond this between the sublingual gland and the genioglossus to open on the top of a small papilla that is situated just lateral to frenulum. The *arterial* supply comes from the external maxillary and lingual arteries, and the *neries* arise in the submaxillary ganglion, the lingual branch of the mandibular nerve and the sympathetics. Each *sublingual gland* consists of a group of glands that lie beneath the mucosa of the floor of the mouth lateral to the frenulum. Each group weighs about 4 gm. The excretory ducts number from 8 to 12 and empty ductletly onto the mucosa, join the submaxillary duct, or unite to form the larger sublingual duct that empties into mucosa with or near the submaxillary duct. The *blood supply*

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SALIVARY GLANDS

EMBRYOLOGY

The salivary glands arise from the buccal epithelium as buds which soon arborize into solid ducts. The terminal portions of these become bulbous and ultimately differentiate into secretory acini,

glands Epidemic parotitis is not a surgical problem and will, therefore, be omitted from discussion *Acute parotitis*, although not extremely common, does fall in the domain of the surgeon It has also been called secondary septic, gangrenous, suppurative phlegmonous, necrotic, postoperative and sympathetic parotitis and parotiditis The most frequent *causative agents* are staphylococci and streptococci, and the route of invasion is said to be by the lymphatics, blood stream, extension from neighboring tissues and ascension up the parotid (Stensen's) duct The latter is by far the most frequent It occurs in patients with poor oral hygiene who are dehydrated and, consequently, have a diminished flow of saliva Such local conditions are found accompanying severe infections, debilitating diseases, metabolic diseases and major surgical operations

The incidence of acute parotitis has been recorded as varying from 0.04 to 0.74 per cent of all patients undergoing major surgical operations The disease occurs at all ages from the first to the ninth decade, but reaches a peak incidence in the fifth decade, it affects females more frequently than males, and it involves each side equally often and both sides in about one-quarter of the cases *Clinically*, there are sudden swelling and pain anterior and inferior to the ear and angle of the jaw, fever to 104°F and leukocytosis to 40,000 The inflammation progresses rapidly, sometimes resulting in gangrene of the entire gland within twenty-four hours Since it is confined within a stout capsule the swelling becomes extremely tense and is not fluctuant *Histologically*, neutrophils are first found within the lumen of the ducts and the acini, and then in the supporting connective tissue Soon there are edema, thrombosis of the capillaries, desquamation of epithelial cells, liquefaction of the tissue and milary abscesses These, as already stated, are followed by gangrene *Treatment* consists of correction of the primary disorder if possible, of attention to oral hygiene, antibiotic (penicillin) therapy, and early adequate surgical drainage *Complications* consist of extension of the pus to the ear, mastoid, pharynx and mouth The *prognosis* should always be guarded for the mortality rate is as high as 60 per cent

Chronic inflammatory lesions of the salivary glands are not common Actinomycosis has rarely been described, and syphilis may occur in the secondary and tertiary stages *Tuberculosis* is most frequent in the parotid gland It may arise as (1) a blood stream metastasis from another focus in the body (2) lymphatic permeation from infected tonsils, external auditory canal and buccal mucosa and (3) a canalicular extension from the mouth It exists as a rapidly or slowly appearing circumscribed fluctuant subcutaneous mass that later becomes tense, shiny, edematous and adherent to the skin It is usually mistaken for a mixed tumor The *diagnosis* is made by biopsy *Treatment* is surgical excision The *prognosis* is good

Mikulicz's Disease—In 1888 Mikulicz reported on a peculiar symmetrical disease of both lacrimal and all the salivary glands that was characterized by a painless tumefaction without a trace of

comes from the sublingual and submental arteries, and the *nerves* are derived from the lingual, chorda tympani and the sympathetics.

Histologically, two types of cells are found in the salivary glands, namely, mucous and serous. *Mucous cells* are irregularly cuboidal, rest upon a basement membrane, disclose terminal bars along their free surfaces, have compressed basilar nuclei, and contain clear cytoplasm that takes a positive red stain with mucicarmin. *Serous cells* are roughly cuboidal and have indistinct borders, round basilar nuclei, and numerous secretion granules between the nucleus and the free border of the cell (Fig. 232). The parotid gland is purely serous; the submaxillary is mostly serous but in some portions is serous and mucous; the sublingual glands are mixed (serous and mucous), while the glands at the root of the tongue and in the palate

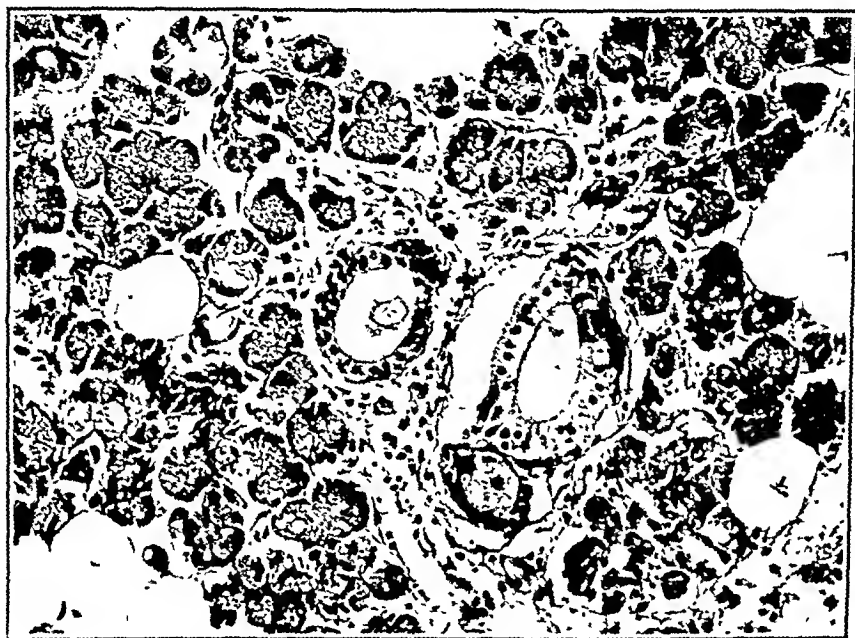


FIG. 232.—Normal parotid gland.

are purely mucous. The excretory *ducts* are lined by a single layer of cuboidal cells. In all glands and ducts, there are present scattered spindle or stellate cells between the basement membrane and the epithelium proper. These are called basal, basket or myoepithelial cells and their function by way of contraction, is to aid in the movement of the secretion.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the salivary glands are uncommon. One or more of the major glands may *fail to develop*; both ducts and acini may be cystically dilated—a condition known as *sialectasis*, and there may be present a *congenital cyst*. The latter is doubtlessly a one-sided development of papillary cystadenoma lymphomatosum and will be considered in connection with this tumor.

Inflammation.—Epidemic parotitis (mumps) and acute parotitis constitute the two chief acute inflam

Tumors—Although lipoma, fibrolipoma, lymphoepithelioma, Hodgkin's disease, lymphosarcoma, melanoblastoma, rhabdomyosarcoma and other tumors of the salivary glands have been described, for all practical purposes there are only two groups of neoplasms that need be considered, namely, mixed tumor with its variant a carcinoma, and papillary cystadenoma lymphomatosum.

Mixed tumor—It has been stated that mixed tumors of the salivary glands constitute about 5 per cent of all neoplasms of the oral and nasal cavity and about 2 per cent of all cancers in man. Their genesis has been and still is a fertile field for speculation. They have been considered (1) as of mesenchymal origin with epithelial elements representing merely the vestiges of the original glands, (2) to



FIG. 234

FIG. 235

FIG. 234—Mixed tumor of the parotid—solid type

FIG. 235—Mixed tumor of the parotid showing foci of necrosis and hemorrhage

be of bidermal origin—cartilaginous and epithelial envelopments of the branchial clefts, (3) to arise from notochordal misplacements and (4) to originate in embryonic rests of the parotid anlage or from adult glandular tissue. The stroma is said to arise from a mucoid degeneration or secretion of epithelial cells or as a result of an organizing action of the tumor cells on the surrounding mesenchyme. The latter theory is the most appealing and fits in with the current concept of the origin of similar tumors in other locations, as for example in the skin. These neoplasms occur at all ages from the second to the ninth decade with an approximate average of forty-four years, are more frequent in males than in females, occur in the parotid gland in from 80 to 94 per cent of all cases, affect each side with equal frequency, and are rarely bilateral. The only symptom

inflammation. As the lesions progressed, they interfered with speaking and eating but, ultimately, they regressed spontaneously. The disorder has since been called *Mikulicz's disease*. It occurs at all ages, but is most common in the fourth decade; it affects men twice as frequently as it does women; it is of several weeks to several years duration, and before completely subsiding it is often characterized by periods of remission. *Grossly*, the lesion occupies the entire gland without distorting its configuration; its consistency if anything is somewhat decreased; its cut surface is homogeneous, pale reddish yellow and less transparent than that of a normal gland, and the vessels are increased only in the septa. *Histologically*, there is a diffuse infiltration with lymphocytic cells with an atrophy or complete disappearance of the acini and often a squamous cell metaplasia of the ductal epithelium (Fig. 233). As the process ages

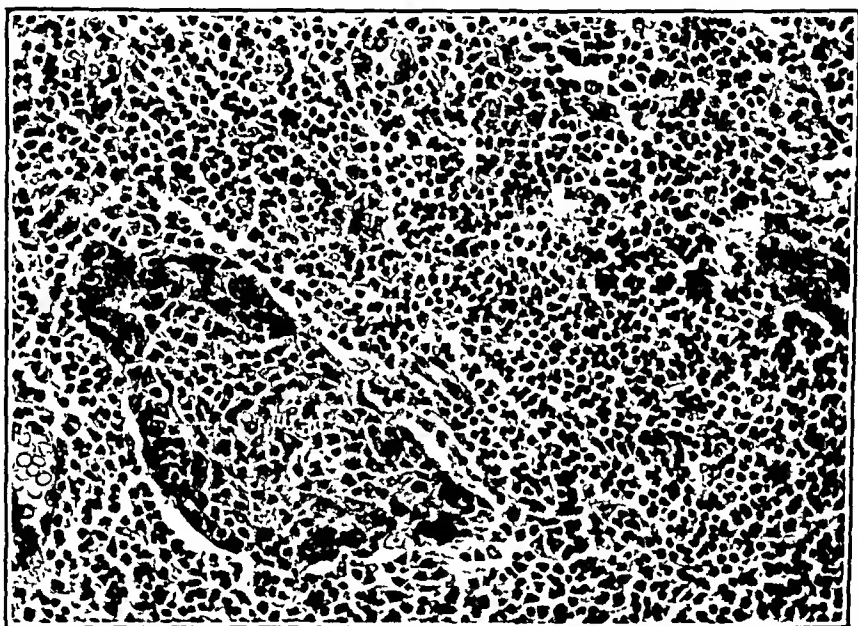


FIG. 233.—Mikulicz's disease of the parotid. There are a diffuse infiltration with lymphoid cells and a squamous metaplasia of the ductal epithelium. $\times 100$.

there is a gradual but diffuse increase of fibrous tissue. The disorder thus appears to be a chronic inflammation, but its cause still remains an enigma. While Mikulicz's patient disclosed an enlargement of both lacrimal and all the salivary glands, I have seen several patients who revealed a perceptible enlargement of the parotid glands alone. Histologically, these lesions were identical with those described by Mikulicz. It appears, therefore, that the *disease can be localized* to one gland or group of glands, and that it need not involve the entire ring. *Other symmetrical enlargements* of the lacrimal and salivary glands caused by leukemia, tuberculosis, syphilis, lymphosarcoma and Hodgkin's disease do not conform to the case originally described by Mikulicz and are, therefore, referred to as *Mikulicz's syndrome*. *Treatment* of Mikulicz's disease has been surgical excision, irradiation therapy, iodides and penicillin. The *prognosis* is good.

Sometimes these masses of cells reveal intercellular bridges and so resemble squamous cells while at other times they are similar to basal cells. Acini may be of two types (1) pseudoacini formed as a result of focal degeneration and complete liquefaction of groups of cells of the basal cell type. In such cases the lumens may still contain varying numbers of intact cells enmeshed in stringy, basophilic, mucoid material. These tumors have often been referred to as cylindromas or low grade adenocarcinoma and, as would therefore be expected, they are prone to metastasize, (Fig 238). They constitute the chief group of cancers of the salivary glands, (2) true acini that duplicate to some extent the acini of the normal salivary glands. They contain a genuine lumen, often filled with mucin, which is surrounded by one or more layers of epithelial cells that rest upon a basement membrane. The stroma is extremely capri-

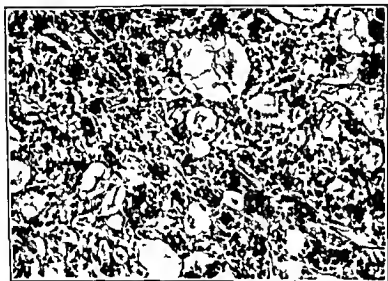


FIG. 238.—Adenocarcinoma of the submaxillary gland that metastasized to the inguinal lymph nodes. $\times 100$

cious. It may be scanty enough so as to be almost imperceptible, or it may be so abundant that the tumor becomes ostensibly a mesenchymal neoplasm. It consists of myxomatous, hyaline, chondroid, osteoid, osseous or calcified tissue. When a benign mixed tumor becomes malignant it is always the epithelial elements that are involved. Aside from the pseudocarcinomatous type of growth already mentioned, a cancerous salivary gland tumor may take on squamous or anaplastic characteristics which exhibit the usual changes of malignancy. Generally, however, such deviations are inconspicuous and one must then rely upon invasion of the capsule and perineural lymphatic channels by tumor cells to establish a diagnosis of carcinoma.

Ordinarily, a mixed tumor of the salivary glands offers no diagnostic problems although it has been confused with an angioma, Hurtle cell tumor, neurofibroma, branchogenic carcinoma, metas-

of note is a swelling usually located in front of or below the ear the duration of which may vary from one month to forty years with an average of seven years. Pain is common and tenderness is rare.

Grossly, the size varies from 0.5 to 10 cm. in diameter. The lesion usually appears unicentric in origin but when smaller it may be seen to rise in several separate foci. Externally it is globular or nodular, and as a rule well encapsulated. It is hard, firm or cystic. Cut surfaces are usually homogeneously white or grey but they may be brown or even somewhat variegated, and sometimes they show foci of necrosis and hemorrhage (Figs. 234 and 235). Cartilaginous material may or may not be recognizable macroscopically. *Histologically*, mixed tumors are quite pleomorphic. Fundamentally, they are composed of two elements—epithelium and stroma (Figs. 236 and 237). The *epithelium* exists in the form of masses, strands, islands or acini of closely packed cells that are sharply demarcated

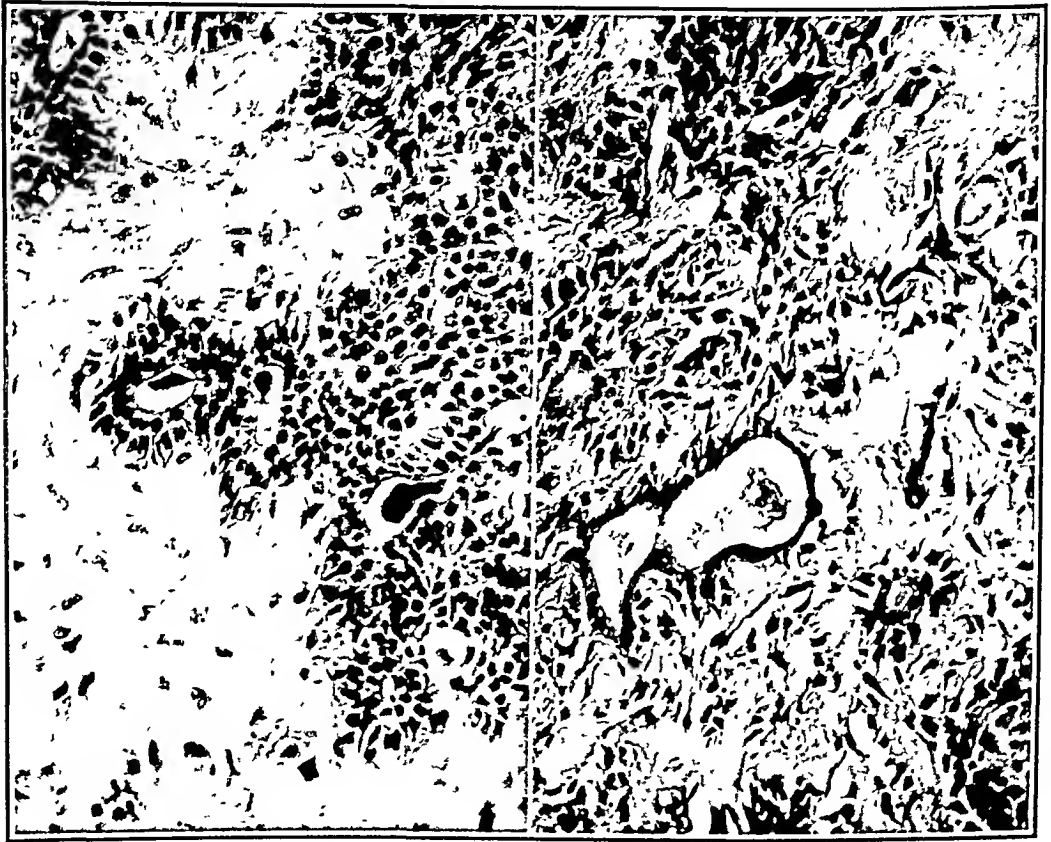


FIG 236

FIG. 237

FIG. 236.—Mixed tumor of the parotid disclosing nests and glands of epithelial cells in a chondroid stroma. $\times 100$.

FIG. 237.—Mixed tumor of the parotid showing a dispersion of epithelial cells in a hyaline stroma $\times 100$.

from, or peripherally intimately blended with, the supporting mesenchyme. The solid collections of cells are polyhedral or spindle shaped, have a moderate or scanty amount of eosinophilic or slightly basophilic cytoplasm, and disclose round or oval hyperchromatic nuclei. Nucleoli are seldom seen and mitoses are absent.

cells (Fig 239) Characteristically, these consist of a double row of tall columnar epithelial cells beneath which there is a single row of basal cells that are aimed on a basement membrane. Sometimes the inner surface is ciliated and at other times the cells are heaped up to form squamous-like structures. The cysts are lined with similar epithelium. The *histogenesis* of this tumor has been the subject of considerable speculation. The most generally accepted theory is that it arises from the first branchial cleft. Other hypotheses are the second branchial pouch, an ectopic tonsil, a lymph node with ectopic buccal epithelium and a vestigial tube of oral mucosa which in animals forms the orbital salivary gland but in man ordinarily disappears. The lesion is usually removed under a mistaken diagnosis of mixed tumor. It does not recur.

Mechanical Disturbances—The only important lesions of the salivary gland that are attributable to mechanical disturbances are fistula, ranula and calculus.

A fistula is an abnormal communication between the gland or its duct and the skin or mucosa. The chief sign is secretion of saliva onto the surface. It occurs in either the parotid or the submaxillary gland, but is important only in the former for in the submaxillary gland it usually heals spontaneously. Its causes are penetrating wounds, surgical operations on or around the glands and their ducts, and suppuration particularly about a calculus. Treatment of ductal fistulas is reconstruction of the ducts, and of glandular fistulas, some roentgen therapy. If these fail, evulsion of the auriculo-temporal nerve will dry up the secretions and seal the opening.

A ranula is a cystic dilatation of one of the submucous glands in the floor of the mouth or of a sublingual gland. Its cause is an occlusion of the corresponding duct, and this is ascribed to a congenital malformation, poor oral hygiene or surrounding stomatitis. It may be painful but more frequently it is accompanied only by disturbances in movements of the tongue. It is as a rule single, situated to one side of the midline, definitely cystic, of a bluish color and may measure as much as 5 cm in diameter. Its wall is thin and covered on the inside with flattened ductal epithelium and on the outside with a few strands of fibrous tissue. It is filled with a colorless mucous fluid. Treatment is complete surgical extirpation.

Calculi in a salivary gland are known as sialolithiasis. The greatest incidence by far is in the *submaxillary gland*. The reasons for this are (1) secretion from this gland is more viscid than it is in the other glands and the ducts, therefore, do not cleanse themselves as readily, (2) the opening of the duct is at a lower level than the gland proper, (3) the duct is long and (4) the orifice being situated in the floor of the mouth is subject to occlusion by food particles and tartar from the teeth. The nucleus of a calculus is any foreign material such as bacteria, sloughed epithelium, tartar, food and unspissated secretion. This is surrounded by calcium carbonate and phosphate salts to form the stone. The calculus may be within the duct, when it is usually smaller and cylindrical with tapering ends, or it may be within the gland proper, when it is larger, globular

tic carcinoma from the kidney and, of course, other enlargements of the salivary glands. *Treatment* consists of complete surgical excision followed by irradiation therapy, if the lesion is cancerous. Without treatment, the tumor extends locally, ulcerates, suppurates but rarely metastasizes, and death is due to hemorrhage from an eroded vessel or to the accompanying cachexia. *Complications* following excision may consist of paralysis of the facial nerve and fistula. The *prognosis* must always be guarded for recurrences occur in at least 25 per cent of cases in as many as forty-seven years after excision.

Papillary cystadenoma lymphomatosum is a benign tumor of the parotid gland that clinically cannot be distinguished from a mixed tumor. Some of the *synonyms* are Warthin's tumor, onkocytoma, orbital inclusion adenoma, adenolymphoma, epitheliolymphoid cyst



FIG 239 —Papillary cystadenoma lymphomatosum showing stalks of lymphoid tissue covered by characteristic epithelium. x 50.

and branchiogenic adenoma. It affects men ten times as frequently as it does women, occurs at all ages, and is of a few months to many years duration. It exists as a unilateral, usually painless, firm, sometimes fluctuating swelling that is confined to the parotid gland and that rarely measures more than 5 cm. in diameter. It is ovoid or round, externally lobulated, and almost always encapsulated. Cut surfaces are often covered with mucinous or brown fluid which, when washed away, leave grey brown or yellowish, trabeculated, underlying tissue. This may contain scattered or numerous small cysts that measure as much as 2 cm. in diameter and, rarely, the entire mass may consist of a single cyst that measures 6 cm. across. The walls of the cysts are smooth and their lumens are filled with brown fluid or inspissated brown material which may contain glistening crystals. *Histologically*, the tumors are composed of a stroma of lymphocytes or well-developed lymph follicles in which there are embedded papillae, tubules or alveoli of epithelial

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and more irregular (Fig. 240). If it is located in the gland proper, it may be symptomless unless it is associated with inflammation at which time the gland is swollen and tender. If it is lodged in the duct, it usually produces partial or complete obstruction to the flow of saliva resulting in swelling of the gland at meal time, or permanently. Sometimes acute infection supervenes in which case there is rapid swelling, pain, tenderness, fever, and trismus. Stone in the duct is almost always associated with a raised, red, prominent ostium of the affected duct. *Histologically*, the gland proper in sialolithiasis discloses edema, neutrophilic infiltration and abscess formation in acute suppurative cases and varying degrees



FIG. 240.



FIG. 241.

FIG. 240 — Calculus in a submaxillary gland.

FIG. 241 — Same case as shown in figure 240. The supporting tissue is fibrous and densely infiltrated with plasma cells and lymphocytes. $\times 200$.

of fibrosis with interstitial plasma cell and lymphocytic infiltration in chronic cases (Fig. 241). *Treatment* consists of removal of the stone, and extirpation of the entire gland only if accompanied by recurrent attacks of inflammation. The *prognosis* is good.

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Chapter IX

ESOPHAGUS

EMBRYOLOGY

THE upper portion of the foregut forms the esophagus. Its lining is derived from the entoderm and from this arise the submucosal glands. The muscle coats develop from the surrounding mesoderm. From the upper and ventral surface, an outpocketing known as the laryngo-tracheal groove is separated from below up to give rise to the trachea and larynx. Normally, the opening between the esophagus and these secondary organs completely disappears. Initially, the esophagus is not only short but its lumen is small. After the fourth week of embryonic life, it elongates rapidly to keep pace with its neighboring organs and after the sixth week its lumen enlarges by proliferation and almost simultaneous vacuolization of the epithelial cells.

ANATOMY

The esophagus is more or less a *straight tube* 23 to 25 cm long that joins the pharynx and the stomach. It starts opposite the cricoid cartilage and the sixth cervical vertebra, pierces the diaphragm opposite the tenth dorsal vertebra and enters the stomach opposite the eleventh dorsal vertebra. *In the neck*, it lies anterior to the vertebral column, posterior to the trachea and between the common carotid arteries. *In the mediastinum*, it courses behind and to the right of the aortic arch, then to the right and finally anterior to the descending aorta. The left bronchus, pericardium and diaphragm lie anterior to its lower portion, the right intercostal arteries pass behind it, and the azygos vein and thoracic duct are in contact with its right lateral border. The arterial supply comes from the thyrocervical trunk, descending aorta, left gastric branch of the celiac artery and from the inferior phrenic branch of the abdominal aorta. A lymphatic plexus invests the tube and drains into the posterior mediastinal nodes. The nerves are derived from the vagus and sympathetic trunks and form one plexus with ganglion cells between the muscle coats and another in the submucosa.

Histologically, the esophagus is composed from within out of a layer of stratified squamous epithelium, a lamina propria composed of connective tissue and a few elastic fibrils, a narrow band of longitudinal smooth muscle fibers called the muscularis mucosa, a layer of dense fibrous tissue known as the submucosa, an inner layer of elliptical and an outer layer of longitudinal muscle fibers, and an outer coat of loose connective tissue called the tunica adventitia (Fig. 242). A constant group of mucous glands connected with the surface by ducts is found in the submucosa, and an inconstant

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in (1) inflammation, ulceration and scarification, (2) hemorrhage from ulceration, (3) the formation of cysts and (4) the development of an adenocarcinoma. An *abnormally short esophagus* occurs when there is a failure of lengthening, and thus a failure of keeping pace with growth of the adjacent organs. It prevents the descent of the stomach into the abdomen resulting in what is known as "thoracic stomach." The latter is considered in more detail under peptic ulcer of the esophagus (p 314) and in the ensuing chapter.

Atresia and tracheo-esophageal fistula are the most important congenital lesions of the esophagus. Formerly, these were merely of academic interest, but perfections in thoracic surgery have reduced the mortality to approximately one-half. This abnormality is said to be as frequent as cleft lip and palate. It results from a failure of the one time normal communication between the esophagus and trachea to occlude, from a failure of the esophagus to expand transversely when its lining cells are proliferating, and from a failure of vacuolization of the newly formed epithelium. With elongation of the esophagus these central cells disappear and the entire structure is represented by a fibrous cord or band. The newborn infant discloses cyanosis, excess frothy fluid at the mouth, inability to swallow, choking and dyspnea after feeding, and vomiting. Examination may reveal an inability to pass a catheter into the stomach, distention of the epigastrium due to an escape of air from the trachea into the stomach, and rapid emaciation and dehydration.



FIG 243 — Atresia of the esophagus with tracheo-esophageal fistula. The upper segment of the gullet ends as a blind diverticulum; the lower communicates with the trachea.

The most common arrangement occurring in from 80 to 91 per cent of all cases consists of a blind upper pouch of the esophagus and a direct communication of the lower segment of the gullet with the posterior portion of the trachea within 1.5 cm. of the bifurcation (Fig 243). The adjacent segments of the esophagus are either connected by a fibrous cord or are completely disunited and separated by as much as 2 cm. Other combinations that occur less frequently are atresia of the esophagus at the same level without a fistula, a fistula without atresia, and a blind lower segment with a fistula between the upper segment and the trachea.

A final clinical diagnosis is established radiologically, either in ordinary roentgenograms or in films after a catheter or iodized oil has been placed within the upper segment. Treatment consists of tying off the fistula and anastomosing the ends of the esophagus. If the latter is impossible due to too wide a separation between the segments, an anterior thoracic esophagus is constructed. Post-

group of glands similar to the cardiac glands of the stomach is present in the tunica propria of the upper part near the level of the cricoid and in the lower part just proximal to the cardiac orifice. The muscle coats in the upper portion are composed of striated muscle, in the middle portion of striated and smooth muscle, and in the lower portion of smooth muscle alone.



FIG. 242.—Normal esophagus showing from above down mucosa, tunica propria, muscularis mucosa, submucosa with glands and a portion of the muscle coat. $\times 50$.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the esophagus may be listed as: atresia with and without tracheo-esophageal fistula, stenosis, absence, doubling, muscular hypertrophy and spasm resulting in dilatation, diverticula, partial or complete membranes or valves, abnormal shortness, and aberrant mucosa. *Aberrant mucosa* is said to occur in from 0.67 to 70 per cent of all cases, is found at all levels, and consists of gastric mucosa and ciliated epithelium. Gastric mucosa results from rests following descent of the stomach and ciliated epithelium is a persistence of the embryonal lining. *Clinically*, this aberrant tissue may result

a hemorrhage. The ulceration is always accompanied by fibrosis which upon contraction may produce stenosis severe enough to occlude the esophageal lumen. *Histologically*, there are varying proportions of superficial necrosis, intermediate granulation tissue and surrounding fibroblastic proliferation. The *diagnosis* is made from a history of typical pain and the demonstration of the ulcer either roentgenographically or esophagoscopically. *Treatment* is at first medical and similar to that for peptic ulcer of the stomach. If this fails it is surgical and, depending upon the circumstances, it consists of dilatation of the constriction, correction of the dia-



FIG. 244.—Scleroderma illustrating atrophy of the epidermis and infiltration of the dermis with hyalinized fibrous tissue. $\times 50$

phragmatic hernia or esophagocenterostomy. The *prognosis* is good for many of the ulcers respond to medical therapy alone.

Lye poisoning is still a frequent cause of inflammation, fibrosis and stricture of the esophagus. It is ingested accidentally by children usually under two years of age, or purposely by adults in suicidal attempts. Immediate *symptoms* consist of pain and difficulty in swallowing. These abate or entirely disappear in from seven to ten days, only to return with increasing severity. The *sites* of the lesions are at the narrow points of the esophagus, namely, the cricopharyngeus, the level of the left bronchus and at the cardiac sphincter. Immediately after swallowing the chemical, the involved mucosa dies and is white in appearance. Histologic examination at this time reveals no pathologic changes whatsoever. On the

operative *complications* consist of leakage at the suture line resulting in mediastinitis, reformation of the fistula, pneumothorax, pneumonia, atelectasis, and constriction at the site of the anastomosis. The *prognosis* must always be guarded for sometimes the operation is successful but the patient dies from associated anomalies that are incongruous with life or, more frequently, from aspiration pneumonia.

Inflammation.—**Non-specific inflammation.**—Non-specific inflammation of the esophagus may be considered under the following headings: acute ulcerative esophagitis, peptic ulceration, lye poisoning and lesions associated with scleroderma.

Acute ulcerative esophagitis concerns the surgeon only insofar as it is a complication of prolonged and difficult operations on patients in poor physical condition. The *genesis* of the lesions is as follows. A slowing of the circulation in the lower part of the esophagus results in a loss of normal resistance whereupon a reflux of gastric juice causes digestion of the devitalized tissue and this opens the way for invasion of bacteria. Trauma from intubation may play a rôle in some cases. The condition affects both sexes with equal frequency and is found at all ages. The only constant *symptom* is vomiting of blood tinged, dark brown, or frankly bloody fluid, but there may also be dysphagia and burning in the esophagus. The *lesions* are usually discovered at necropsy. The cardiac sphincter is relaxed; the lower one-half or one-third of the esophagus is dilated; the lumen contains gastric contents; the rugae are usually erased, and the mucosa discloses simple congestion and petechiae or frank ulcerations. The latter are small or large, longitudinal or irregular, superficial or penetrate the entire thickness of the wall, and are usually associated with considerable edema of the surrounding tissue. *Histologically*, there are a replacement of the mucosa with cellular débris with or without excavation of the underlying tissue, an engorgement of the adjacent capillaries, edema of the adjoining connective tissue, and varying degrees of neutrophilic, eosinophilic, plasma cell and erythrocytic infiltration. A correct *diagnosis* is rarely established before necropsy examination and *treatment* is therefore directed towards the original disease.

Peptic ulceration of the esophagus is also dependent upon the presence of gastric juice either as a result of secretion from ectopic gastric mucosa or in the presence of a thoracic stomach such as is consequent to a short esophagus. The lesion affects males and females with equal frequency, and it usually occurs after the age of thirty years. *Symptoms* consist of pain in the lower portion of the mediastinum or epigastrium that is aggravated by food and that may radiate down the arms, of intermittent vomiting of dark brown or bright red blood, and of varying degrees of dysphagia. The *ulcer* is located in the lower third of the esophagus. It may be round or oval and a few millimetres in diameter or it may be irregular, large and encircle the entire lumen. The smaller defects are frequently confined to the superficial layers, but the larger lesions may penetrate the entire wall to produce a mediastinitis, a bronchial, pleural or pericardial fistula, or with erosion of a vessel

The *location* of the lesion depends upon the mode of infection. If the lesion is primary or part of a general dissemination any portion may be affected, if it is an extension from the pharynx the upper portion is involved, if the infection is grafted upon a previous mucosal lesion the site will depend upon the location of the predisposing disease, and if it is an extension from tuberculous lymphadenitis or osteomyelitis the level will also depend upon the level of the primary focus. *Grossly*, primary mucosal lesions are ulcers that are often altered by the preceding disease or by secondary infection. Lesions that extend from the peri-esophageal tissue, if seen early at postmortem or by the esophagologist, will disclose a raised reddened mucosa with a soft, prominent, bleb-like, yellow center that soon ulcerates and discharges caseous or yellowish pus. This leaves an excavated ulcer with irregular undermined edges. With healing there is deposition of fibrous tissue which may eventually result in stenosis of the lumen. *Histologic* examination discloses tubercles or tuberculous granulation tissue. The *diagnosis* is made by biopsy and by isolating the tubercle bacillus. *Treatment* consists of dilatation for organic or spastic stenosis and of general antituberculosis measures when necessary. The *prognosis* is good if the lesion is localized to the esophagus but is poor if it is part of a general infection.

Syphilitic lesions of the esophagus are of the tertiary type and are almost always confined to the gummatous variety. They are found in adults, and when they encroach upon the lumen they produce dysphagia. They are located in all portions of the esophagus but are probably more frequent in the lower two-thirds. The disease may be *primary* in the gullet or it may be *secondary* to a lesion in an adjacent organ such as the liver and diaphragm. *Grossly* and *histologically*, a gumma in the esophagus is the same as one in other organs (see Chapter I). A *diagnosis* is made from a history of dysphagia, a positive serologic test for syphilis, the presence of esophageal obstruction demonstrable radiologically and esophagoscopically, and biopsy. *Treatment* consists of antisyphilitic therapy and dilatation of the esophagus when stenosis develops.

Tumors—Neoplasms of the esophagus except for carcinoma are rare. Classified histogenetically there have been described from the epithelium a papilloma, adenoma, cyst and carcinoma, from connective tissue a fibroma, polyp and myxofibroma, from blood vessels a hemangioma and hemangioendothelioma, from fat tissue a lipoma, from mesodermal elements as a result of metaplasia an osteochondroma, from muscle a myoma including both a leiomyoma and rhabdomyoma, from aberrant tissue an adenoma of the thyroid, and from distant organs metastatic tumors. Of the benign tumors a myoma alone occurs frequently enough to merit further discussion and the only malignant tumor worthy of note is carcinoma.

Myomas—Myomas of the esophagus affect males twice as frequently as they do females and, although they occur at all ages, their peak incidence is in the seventh decade. Many of them are asymptomatic and are discovered only as incidental findings at necropsy. Others produce *symptoms* of a few months or many

contrary the epithelial cells are in a perfect state of preservation for the sodium hydroxide has fixed them in situ. Within a few hours, however, the epithelium sloughs, ulcers form and there develop intense edema and leukocytic infiltration of the submucosa and muscle wall. After the fourth day, the acute inflammation wanes and is superseded by fibrosis which constricts enough to produce obstructive symptoms by the thirtieth day. In addition to this mechanical stenosis, an element of spasm, consequent to secondary inflammation from ingested food, always aggravates the occlusion of the lumen. The *diagnosis* of lye poisoning is usually easy because of associated burns of the face and mouth. Immediate *treatment* consists of an antidote of weak acid to be followed by dilatation of the esophagus by an expert esophagologist after the fourth day. Dilatation is also the treatment if seen for the first time during the cicatricial stage. The *death rate* is about 10 per cent and is due to the poisoning itself or to perforation of the esophagus with mediastinitis either as a result of ulceration itself or injudicious treatment.

Scleroderma is associated with an esophageal lesion in about 10 per cent of all cases. Scleroderma is a generalized disease with initial manifestations in the *skin* in the form of raised erythematous areas. This transient inflammatory change is soon replaced by a progressive deposition of hyalinized, acellular fibrous tissue both in the dermis and subcutaneous tissues (Fig. 244). A similar change occurs in other locations of the body among which is the *submucosa* of the *esophagus*. This infiltration of the gullet results in a retardation or lack of motility, in stenosis of the lower part, and in dilatation. Added to the mechanical obstruction there is usually a disturbance of the autonomic nervous system which results in cardiospasm. *Symptoms* consist of dysphagia, of a "lump" in the esophagus and occasionally of pain and burning on swallowing. *Grossly*, the esophagus is dilated; the rugae are absent, and the mucosa is thick and glossy, leukoplakic or ulcerated. *Histologically*, there are a massive submucosal and intermuscular deposition of fibrous tissue, an infiltration with lymphocytes, fragmentation of the elastic fibers, and atrophy of the muscle. *Treatment* consists of dilatation of the esophagus when obstruction develops. The *prognosis* is poor for by the time lesions occur in the gullet the disease is usually far advanced.

Specific Inflammations.—Specific inflammations of the esophagus are rare and consist of tuberculosis, syphilis, actinomycosis and blastomycosis. The former two are much more frequent than the latter of which only isolated cases have been reported.

Tuberculous esophagitis is usually the result of *extension* from tuberculosis of adjacent lymph nodes, vertebrae or pharynx. Less frequently it arises from swallowed tubercle bacilli implanted upon a pre-existing lesion of the mucosa and rarely does it develop as a hematogenous infection. The onset is usually gradual but, occasionally, it is abrupt and is ushered in by dysphagia and odynophagia. Roentgenograms of a barium filled esophagus will show a deformity or stenosis of the lumen and sometimes calcific deposits in an extra luminal mass. These represent calcified lymph nodes.

The location of the lesion depends upon the mode of infection. If the lesion is primary or part of a general dissemination any portion may be affected, if it is an extension from the pharynx the upper portion is involved, if the infection is grafted upon a previous mucosal lesion the site will depend upon the location of the predisposing disease, and if it is an extension from tuberculous lymphadenitis or osteomyelitis the level will also depend upon the level of the primary focus. *Grossly*, primary mucosal lesions are ulcers that are often altered by the preceding disease or by secondary infection. Lesions that extend from the peri-esophageal tissue, if seen early at postmortem or by the esophagologist, will disclose a raised reddened mucosa with a soft, prominent, bleb-like, yellow center that soon ulcerates and discharges caseous or yellowish pus. This leaves an excavated ulcer with irregular undermined edges. With healing there is deposition of fibrous tissue which may eventually result in stenosis of the lumen. *Histologic* examination discloses tubercles or tuberculous granulation tissue. The diagnosis is made by biopsy and by isolating the tubercle bacillus. *Treatment* consists of dilatation for organic or spastic stenosis and of general antituberculous measures when necessary. The *prognosis* is good if the lesion is localized to the esophagus but is poor if it is part of a general infection.

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Others produce symptoms of a few months or many

years duration that may consist of dysphagia, regurgitation of food or even of the tumor itself if it is pedunculated, substernal or epigastric discomfort, and loss of weight. *Grossly*, the growth is usually single, occurs at all levels with a predilection for the lower one-third, varies in size from a few millimeters to many centimeters, and is usually pedunculated sessile or intramural, but it occasionally encircles the lumen. It is sharply demarcated, elongated, round, oval or bossed, has a false capsule of connective tissue, is firm, and its cut surfaces are composed of greyish white avascular tissue (Fig. 245). *Histologically*, the tumor varies according to

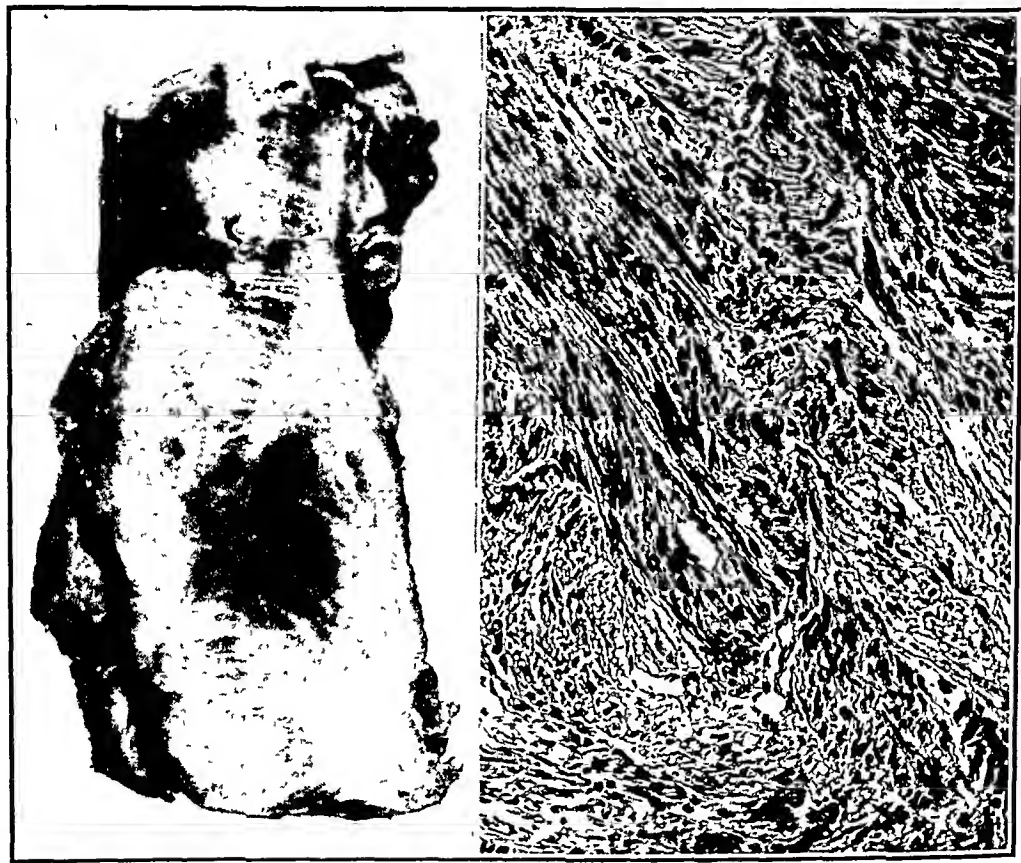


FIG 245

FIG 246

FIG. 245.—Longitudinal section of a leiomyoma of the lower portion of the esophagus
 FIG. 246.—Same case illustrating interlacing bundles of smooth muscle. x 100

the level. In the upper third it is usually a rhabdomyoma, in the middle third a rhabdomyoma, a leiomyoma or a mixture of the two, and in the lower third a leiomyoma. The latter is the most frequent. It is composed of bundles of smooth muscles coursing in all directions (Fig. 246). The cells are larger than normal and exhibit a moderate amount of spindle shaped cytoplasm with rod or spindle shaped nuclei. This structure is, however, usually modified, for the tumors frequently undergo hydropic, fatty, hyaline or calcific degeneration. The *diagnosis* is established (1) radiologically, particularly by stereoroentgenograms and fluoroscopy, (2) esophagoscopically and (3) whenever possible by biopsy.

Treatment of small asymptomatic tumors is unnecessary, of pedunculated growths, it is endoscopic removal, and of symptomatic mural or extramural neoplasms, it is surgical extirpation. The *prognosis* is good.

Carcinoma—Cancer of the esophagus constitutes about 6 per cent of all malignant tumors, produces more than 2000 deaths a year in the United States, and in men is exceeded only by carcinoma of the stomach, prostate, lung, and rectum. Its *causes*, as in cancer of other organs, are not known but the following are thought to play an etiological role: (1) a hereditary predisposition for it is said that the disease predominates in Russian and Polish Jews,



FIG 247

FIG 248

FIG 247—Early carcinoma of the esophagus showing only a wrinkling and granularity of the mucosa

FIG 248—Scirrhus carcinoma lower end of the esophagus

(2) congenital anomalies such as short esophagus, (3) a nervous temperament which results in spasm, (4) leukoplakia to about the same extent as it is a factor in the mouth and (5) repeated trauma at points of physiological narrowing as the pharyngo-esophageal junction, at the level of the left bronchus and at the cardia. Irritation is produced by improperly masticated food, hot foods, alcohol and tobacco. Cancer of the esophagus prevails in males over females in the proportion of three to one, and although it is found at all ages from the second to the ninth decade its peak incidence is around fifty years. *Symptoms* are not produced until there is some encroachment upon the lumen. Initially, there may

be only a vague sensation after taking food or a feeling of its temporary lodgement in the gullet. Later there are dysphagia, pain (when the tumor extends to the aorta and vertebra), loss of weight, vomiting, hoarseness (from paralysis of recurrent laryngeal nerves), hematemesis and cough. The duration of symptoms before seeking medical aid varies from three weeks to two years.

The *lesions* occur with about equal frequency in the middle and lower thirds, and these areas combined, account for over 80 per cent of all esophageal carcinomas. *Grossly*, the growth starts as a mere roughening or granularity of the mucosa that in the unfixed specimen may be difficult to distinguish from normal

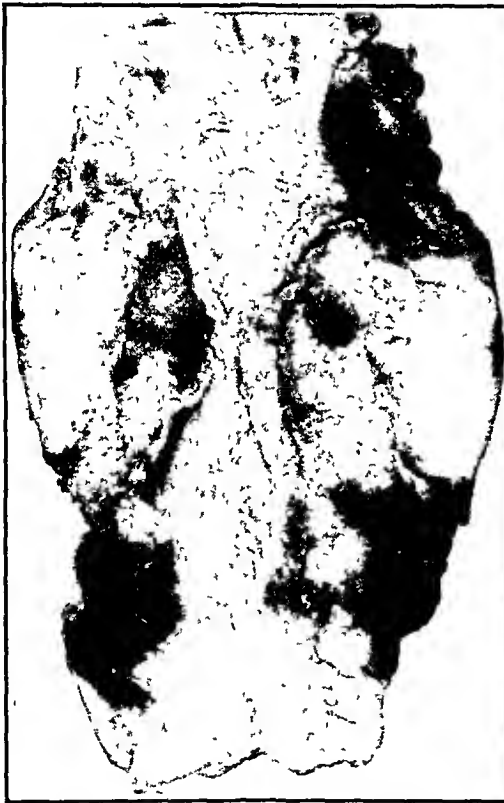


FIG. 249.

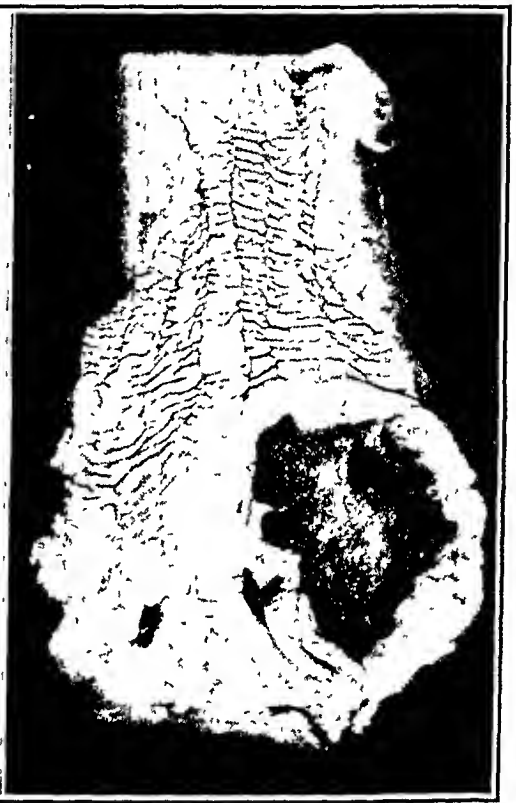


FIG. 250.

FIG 249.—Fungating carcinoma of the mid portion of the esophagus.

FIG 250.—Ulcerating carcinoma of the lower portion of the esophagus.

wrinkling (Fig. 247). Soon, however, the picture changes for the tumor infiltrates into the submucosa, whence it spreads by lymphatic channels to other levels and by extension to the muscle coats. Simultaneously, the surface sloughs producing ulcers of varying configuration, size and depth. Henceforth the neoplasm takes on one of three forms with transitions from one to the other. (1) *Scirrhus* when it is accompanied by moderate or extensive fibrosis to produce an extremely firm grey granular mass. This has a tendency to encircle the lumen and then extend for considerable distances along the length of the esophagus ultimately producing a cylindrical tumor that usually measures as much as 10 cm. in length and 3 to 4 cm. in diameter (Fig. 248). The ends

of the neoplasm are sharply demarcated, the sides extend to and beyond the muscle coats, its inner portion is superficially ulcerated, and the lumen is markedly or completely obliterated (2) *Papillary* when the tumor fungates into the lumen to produce a cauliflower-like growth (Fig 249) It remains confined to a narrower segment of the wall, is grey, considerably softer, more friable and consequently discloses a central excavation filled with necrotic material Its base is usually sessile but it may be pedunculated Because it grows into the lumen it distorts the shape of the gullet, but the unaffected segment of the circumference is merely stretched over the growth resulting in a maintenance of a patent lumen for a considerable length of time (3) *Ulcerating* medullary in which case the tumor, being accompanied by less fibrosis than the scirrhous variety, is similar to the papillary type, except that instead of growing into the lumen it extends into the wall of the esophagus (Fig 250) These growths reveal early and deep ulceration which keeps pace with the advancing edge of the cancer and consequently may produce perforation before the growth is scarcely more than 2 cm in diameter *Histologically*, 95 per cent of esophageal carcinomas are of the stratified squamous variety The transition from normal to cancer tissue is usually abrupt If seen early, the tumor is confined to the mucosa (intraepithelial carcinoma or carcinoma in situ) but if seen later, it infiltrates the tunica propria and deeper layers in the usual manner (Fig 251) The neoplasm grows in cords, sheets or nests in the better differentiated growths and more diffusely in the more anaplastic varieties In the former the cells are polygonal, sharp, have moderate or abundant cytoplasm and round, oval or irregular hyperchromatic nuclei Keratinization and pearl formation may be conspicuous or entirely absent The more anaplastic cancers are considerably less frequent and exist as irregular collections or single hyperchromatic polyhedral, spindle or otherwise bizarre cells with intensely hyperchromatic nuclei Sometimes they bear some resemblance to sarcoma and have, therefore, been called *carcinosarcomas* As already stated the supporting fibrous tissue may be scanty or it may be abundant It is usually dense, acellular and is almost always infiltrated with plasma cells and lymphocytes Most of the remaining 5 per cent of esophageal cancers are adenocarcinomas that originate in the cardia of the stomach These may extend for considerable distances cephally to involve even the middle third of the gullet They are composed of irregular acini lined with columnar or cuboidal cells that have basilar nuclei and varying degrees of vacuolization of the cytoplasm (Fig 252) A third type of cancer that is extremely rare, is the basal cell carcinoma It is almost always found in the lower third of the esophagus

Carcinoma of the esophagus usually spreads first by direct extension to the trachea, mediastinum, bronchi, aorta, pleura, lung, stomach, diaphragm, larynx, thyroid and pericardium Fifty per cent of all cases show invasion of some of these structures at the time of operation These extensions, if accompanied by penetrating ulceration, may eventuate in perforations into the neighboring

structures resulting in severe infections or fatal hemorrhage. Lymphatic metastasis accounts for spread of the cancer to the esophageal, bronchial, tracheal, abdominal and supraclavicular nodes, whereas blood stream dissemination involves the following organs in decreasing order of frequency: lung, pleura, liver, kidney, stomach, bones, thyroid, peritoneum and almost every other organ and all tissues. It should be noted, however, that the lesion nevertheless remains localized for a considerable time as indicated by the fact that 40 per cent of all cases coming in necropsy do not show metastasis.

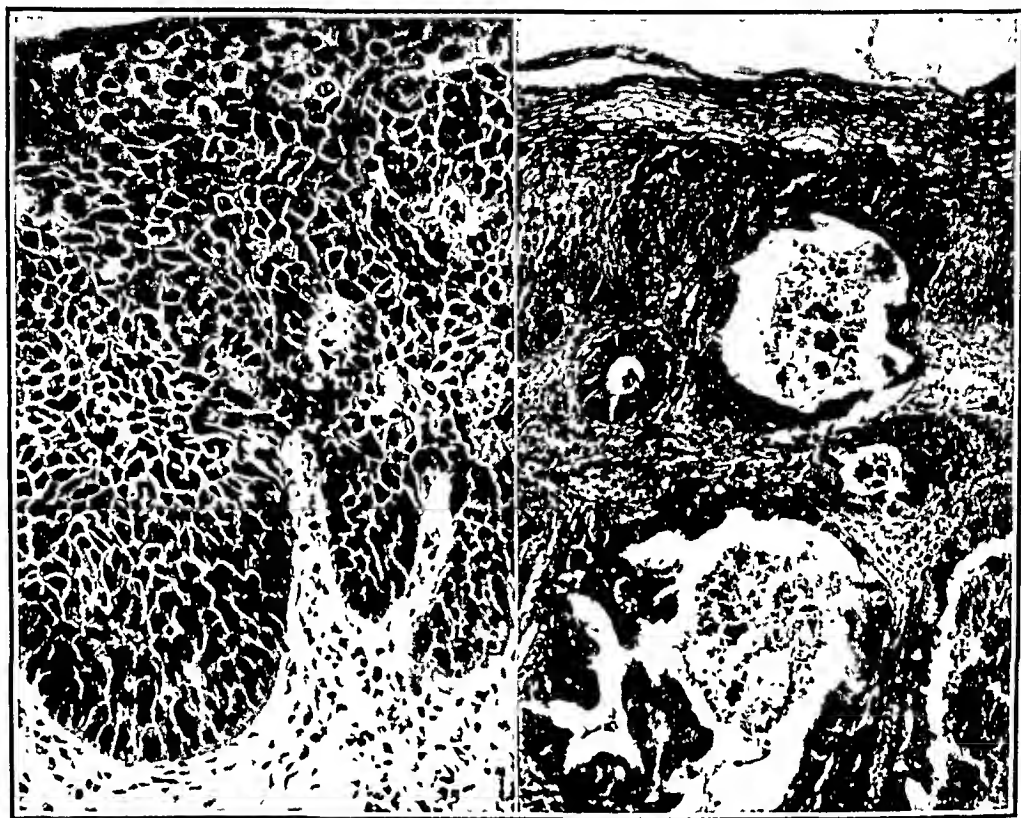


FIG. 251.

FIG. 252.

FIG. 251.—Carcinoma in situ. Same case illustrated in Fig. 247. Note that the cancer is still confined by the basement membrane. x 100

FIG. 252.—Adenocarcinoma of the esophagus. The acini are infiltrating the submucosa. x 50

Cancer of the esophagus should be suspected in any patient presenting symptoms referable to the gullet and, particularly, if the patient is a male. The *diagnosis* is confirmed roentgenologically, esophagoscopically and by biopsy. *Treatment* is extremely unsatisfactory. Irradiation has been given a thorough trial but has not in a single case produced a cure. It may, however, reduce the infection, thereby temporarily relieving the obstruction and decreasing the morbidity. Gastrostomy in some cases accomplishes the same thing, but as would be expected is only temporary. Esophagectomy followed by an anastomosis between the remaining esophageal segment or by a plastic anterior thoracic esophagus offers the only hope. Because the organ is inaccessible, devoid of a serosa,

has a poor collateral circulation and lacks redundancy, this operation is formidable and at best is attended by an immediate *mortality* of 40 per cent. Seventy per cent of the survivors have a chance of living more than one year. Without treatment the average duration of life after symptoms develop is seven months, treated by gastrostomy it is 10.4 months, and following irradiation therapy it is 9.3 months.

Mechanical Disturbances—Mechanical disturbances of the esophagus may be divided into the following categories: diverticula, Plummer-Vinson syndrome, occlusion of the cardia, varices, foreign bodies, perforations and fistulas, and dysphagia.

Diverticula—Diverticula of the esophagus are customarily divided into two types—traction and pulsion. *Traction diverticula* occur following peri-esophageal inflammation with contraction of the resultant adhesions. Usually the inflammatory process is tuberculous lymphadenitis and consequently, the lesion is most frequent in the anterior wall just inferior to the bifurcation of the trachea. The diverticulum is conical in shape, has a wide mouth, and measures a few millimeters or several centimeters in depth (Fig 253). Its mucosa is ordinarily intact but occasionally, it is ulcerated and thus may eventuate in complete perforation. As a rule there are no symptoms. The lesion may be found during a routine roentgenographic study of the esophagus or more frequently it is encountered as an incidental finding at necropsy. *Pulsion diverticula* on the other hand are of clinical significance. Although they may occur at any point along the esophagus, they are so frequent at the *pharyngo-esophageal junction* that the term has almost become synonymous with an outpocketing of the upper portion of the gullet. The lesion is a herniation of the mucosa between weak spots in the musculature. Its *genesis* is a neuromuscular incoordination—a failure of the cricopharyngeus to relax following the contraction of the inferior constrictor. This increases the intra-luminal pressure and results in a bulging of the mucosa between the muscle fibers. The most common site is between the cricopharyngeus and the inferior constrictor muscles, but the herniations may also occur between the cricopharyngeus and the circular fibers of the upper portion of the esophagus proper and rarely, between the fibers of the lower portion of the inferior constrictor muscle itself. The condition is usually seen after the age of forty years, it affects men in over 80 per cent of cases, and the duration of symptoms varies from a few months to over forty years. Initially, there may be only an occasional lodging of food in the throat, but later there are noisy deglutition, increasing dysphagia, unpredictable regurgitation of food which may result in aspiration pneumonia or pulmonary abscess, vomiting, and loss of appetite and weight. Rarely, a compressible tumor may be felt in the neck.

The *diverticulum* is found more often on the left side. At first it is present as a small dimple but this soon enlarges and elongates to form an elongated sac with a narrow or broad neck that may measure as much as 8 cm. in length (Fig 254). Its course is downwards and it produces dysphagia by compressing the lumen of the esophagus.

from without and, because of its drag upon the gullet, by reducing the mouth of the esophagus to a narrow slit. *Histologically*, it is composed from within out of squamous epithelium, a submucosa that may be infiltrated with lymphocytes and plasma cells, and a few patches of muscle tissue. Infrequently, the mucosa may be ulcerated and, rarely, it may become cancerous.

The *diagnosis* is suspected from the clinical history as outlined and is confirmed roentgenographically after ingestion of barium and esophagoscopically. *Treatment* consists of surgical removal. Post-operative *complications* that may arise are mediastinitis, hemorrhage, recurrence of the diverticulum, pneumonia (for preoperative bron-



FIG. 253.

FIG. 254.

FIG. 253 —Traction diverticulum of the esophagus
FIG. 254 —Pulsion diverticulum at esophago-pharyngeal junction.

chitis is frequent), fistulas and wound infection. With proper surgical technique, however, these complications are minimal and the *prognosis* is good.

Plummer-Vinson Syndrome.—This syndrome has also been described under the following captions: crico-pharyngeal spasm, functional dysphagia, spasmodic stenosis, globus hystericus, hysterical dysphagia and esophageal neurosis. It is usually found in women between the ages of forty and fifty years, and consists of an inability to swallow solid food, anemia, glossitis, splenomegaly and achlorhydria. It appears as though the *dysphagia* is the initiating factor and the remaining findings are consequent to an inadequate intake of food. The causes of the dysphagia consist of hysteria,

painful ulcers and fissures at the entrance of the esophagus that result in reflex spasm, degeneration and inflammation of Auerbach's plexus which prevents relaxation of the sphincter in the first act of swallowing, webs and bands of fibrous tissue. The anemia is of the hypochromic microcytic type in which erythrocytes number from 2,500,000 to 4,000,000 per c mm and the hemoglobin ranges from 25 to 60 per cent. The tongue is smooth, red, painful and the papillae are atrophic. Splenomegaly and achlorhydria are not present in all cases. In many patients, *esophagoscopy* reveals no lesions, in others, it discloses bands of fibrous tissue that run in all directions, and in others still, there may be only a resistance to the passage of the instrument which is readily overcome, but upon withdrawing the esophagoscope a careful examination will disclose bleeding cracks or tears in the mucosa. Despite the many cases of the syndrome recorded in the literature, there has been an extreme dearth of material available for *pathologic* examination. In the reported cases there have been described a thinning of the epithelium of the esophagus without ulceration, a replacement of the lamina propria and submucosa with collagenous fibrous tissue, an infiltration of the same layers with lymphocytes, and degeneration atrophy and moderate fibrosis of the muscle coats. *Treatment* consists of dilatation of the constriction. The *prognosis* is good.

Occlusion of the Cardia—Occlusion of the cardiac end of the esophagus has been termed cardiospasm, ectasia, idiopathic dilatation, achalasia, phrenospasm and fibrosis of the lower end. It is about one-third as common as carcinoma, occurs at all ages from birth to the eighth decade, and is somewhat more frequent in women. The *causes* of the occlusion are doubtless very diverse and may be grouped under the following five headings: (1) A true *achalasia*—a neuromuscular incoordination whereby the cardiac end fails to relax. This is due to the unopposed action of the sympathetic fibers following a destruction of Auerbach's plexus. Achalasia is the most common cause of the stenosis. This is not merely a theory for changes in the myenteric plexus have been noted in man and the disease has been reproduced in cats, dogs, monkeys and rabbits by sectioning the vagus nerves. (2) Simple *spasm* of the cardiac end of the *esophagus*. Credence for this theory lies in the fact that frequently the patients are of a nervous temperament, that the condition often dates to some shock as operation or accident, and that spinal anesthesia completely relaxes the tonicity of the gullet allowing free passage of food into the stomach. In other cases the spasm is considered to be a reflex irritation from lesions in the posterior peritoneum, ulcers of the stomach and duodenum, and cholelithiasis. (3) *Gluing* together of the prominent *esophageal* folds and fibrosis of the submucosa. These changes are said to be secondary to inflammation of the gall bladder, pneumonia, bacteremia and, locally, to infection of the esophageal glands and thrombosis of the veins with resulting mucosal ulceration. (4) A congenital increase in length of the esophagus to form an S shaped organ—a *dolicho-esophagus*. These patients present no spasm of the cardiac end the obstruction being due to hydrostatic pressure upon the sagged

walls of the gullet. (5) A *spasm* of the crura of the *diaphragm*. Initially, *symptoms* consist of a momentary sticking of the food in the lower end of the esophagus or inability to swallow cold fluids. Gradually, there develop substernal or epigastric discomfort or pain, regurgitation of partly digested alkaline food, dyspnea and paroxysms of nocturnal coughing from aspiration of esophageal contents.

Grossly, the esophagus immediately above the diaphragm is constricted to produce a neck that measures from 1.5 to 4.5 cm. in length (Fig. 255). Above this point the lumen is dilated to a capacity of 2800 c.c. It is redundant and curved upon itself. The



FIG. 255 —Achalasia esophagus.

wall is leathery and thickened to as much as 1 cm. The mucosal folds are erased and the mucosa may be superficially ulcerated. Frequently, it is covered with irregular, patchy, grey material. *Histologically*, there are superficial keratosis, erosion or frank ulceration. The submucosa and varying depths of the muscle coats are infiltrated with fibrous tissue, plasma cells and lymphocytes (Fig. 256). In some cases, there is also partial or complete replacement of the ganglion cells of Auerbach's plexus with fibrous tissue or inflammatory cells.

The *diagnosis* should be suspected after eliciting the typical history, and is easily confirmed roentgenologically when barium in the esophagus discloses the characteristic bottle-like deformity.

Esophagoscopy should always be performed to rule out a carcinoma or other tumor. *Treatment* consists of (1) rest, sedatives, antispasmodics and thiamine chloride, (2) dilatation of the constriction which usually gives symptomatic relief after one or two manipulations and (3) various surgical procedures in intractable cases the most popular of which are esophago-gastrostomy and sympathectomy. The *prognosis* is good, although cancer has been described as a complication.

Varices—The esophageal veins of the lower portion of the gullet unite with the coronary veins and the vasa brevia of the stomach to form one of the links between the portal and systemic circula-

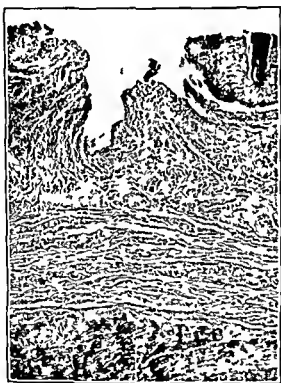


FIG. 256—Same case illustrated in fig. 255 showing ulceration of the mucosa and fibrosis and inflammation of the submucosa. $\times 25$

tions. They are surrounded only by the loose connective tissue of the submucosa which offers little support and allows dilatation whenever the intraluminal pressure is increased. Consequently, varices develop as a result of obstruction of the portal and splenic veins and are, therefore, a common finding in Banti's disease and cirrhosis of the liver. Their clinical significance lies in the fact that they erode the mucosa, rupture and frequently result in fatal hemorrhage. *Symptoms*, therefore, consist of hematemesis and melena. *At necropsy*, they are seen as raised, tortuous, blue submucosal ridges that run in the longitudinal axis of the lower portion of the esophagus. Upon removal from the body, they have a tendency to collapse although sometimes they are thrombosed.

In cases of fatal hemorrhage the bleeding point can be identified in about one-half of the cases. The *diagnosis* is made from a history of hematemesis or melena in conjunction with other signs and symptoms of Banti's disease or cirrhosis of the liver, and is corroborated roentgenographically and esophagoscopically. *Treatment* is unsatisfactory and consists of a bland diet, splenectomy in Banti's disease, ligation of coronary veins to interrupt the collateral circulation, omentopexy to establish a collateral circulation and injection of the varices with sclerosing solutions. The *prognosis* is poor not only because of the frequently fatal hemorrhage but also because the primary disease is rapidly progressive.

Foreign Bodies.—Foreign bodies in the esophagus are about as frequent as they are in the respiratory tract. In *adults*, the most common objects are bones and dentures. The former are available in carelessly prepared food and are frequently swallowed by people with dentures. Because they are sharp and injure the wall, they produce pain upon swallowing and the patients, therefore, seek relief relatively early. In *infants* and *children*, the most common objects are open safety pins with the keeper and point directed upwards. These patients too are brought to the physician early. Coins, discs and buttons are also frequently found in children and infants, but because they are round they produce little trauma and their sojourn may be as long as nine months. In such cases a marked peri-esophageal swelling produces tracheal compression resulting in dyspnea as the outstanding symptom. Aside from these, any objects in the line of hardware, toys or jewelry which are large enough to be swallowed are also encountered in the esophagus. *Complications* result from the objects themselves or from attempts at removal. Chief among these are perforation and infection. The *diagnosis* is made from the history, roentgenographically particularly in radio-opaque objects, and esophagoscopically. *Treatment* consists of removal with the aid of the esophagoscope. In the hands of an expert, the *prognosis* is good.

Perforations and Fistulas.—Fistulas of the esophagus are *congenital* and acquired, while perforations are always acquired. Since developmental lesions have already been considered, they are not included in the following discussion. *Acquired* fistulas and perforations can occur at all ages from a few days post-natally to the eight or ninth decades of life. Their causes in approximate order of frequency are: (1) *Malignant tumor*. This is almost always a carcinoma and, in the majority of cases, is primary in the mid portion of the esophagus. Less commonly, the lesion originates in the tracheo-bronchial tree, thyroid or is secondary in the mediastinal lymph nodes. (2) *Infection*. The most common of these is tuberculosis of lymph nodes which caseates and erodes into the esophagus, and, less frequently, tuberculosis primarily within the wall of the gullet itself or a tuberculous empyema. Other infections that may produce esophageal perforations and that are located either within the esophagus or in adjacent structures are syphilis, actinomycosis, blastomycosis and pyogenic esophagitis or empyema. (3) *Trauma*. This includes swallowed objects already enumerated, ingested

corrosive substances, instrumentation such as the passage of bougies or esophagoscope, crushing injuries and cutting and gunshot wounds (4) Esophageal *diverticula* either of the traction or pulsion type in which there is inflammation and ulceration of the wall (5) Acute *ulcerative esophagitis* which has already been discussed under inflammations Perforations of the gullet are, as a rule, followed by localized infection, abscesses and fistulas The latter communicate most frequently with the trachea and bronchi and less frequently with the pleura skin, pericardium, and one of the major vessels

Symptoms will, of course, depend upon the type of lesion, its location and the organs involved Accordingly, there may be varying degrees of pain and difficulty in swallowing, paroxysms of cough and dyspnea after eating, vomiting of purulent material, food in the sputum, cachexia, hemorrhage due to erosion of a vessel, emphysema or symptoms referable to pneumothorax or pericarditis *Treatment* is directed towards maintaining the nutrition and adequate drainage The esophagus is put at rest by way of an indwelling Levine tube or by gastrostomy, the ostium may be sealed by applying crystals of sodium hydroxide, the tract may be excised and chemotherapeutic and antibiotic drugs are administered Since the majority of cases are due to carcinoma, the *prognosis* is poor

Dysphagia is, of course, a symptom and not a disease Its *causes* are protean and may briefly be enumerated as follows (1) *congenital* abnormalities in the form of stenosis, atresia, diverticula, membranes, spasm and muscular hypertrophy, (2) *inflammations* (a) of the esophagus in the form of acute ulcerations, that associated with scleroderma, and chronic granulomatous lesions such as tuberculosis, syphilis and fungus diseases and (b) of the mediastinum in the form of cellulitis or abscess, (3) *tumors* of the esophagus either benign or malignant, and tumors of adjacent lymph nodes either primary or secondary In this category may also be included aneurysm of the aorta, (4) *mechanical disturbances* which include foreign bodies, fibrosis, acquired diverticula and neuromuscular disturbances, either in the form of spasm from local irritation or degeneration of Auerbach's plexus or in the form of paralysis from a lesion in the medulla oblongata

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precedes the pyloric orifice. The *arterial* supply is derived from the left gastric of the celiac artery, the right gastric and right gastroepiploic of the hepatic artery and the left gastroepiploic and short gastric of the splenic artery. The *neries* are the right vagus distributed to the postero-inferior surface, the left vagus to the antero-superior surface and numerous branches from the celiac plexus of the sympathetics to both surfaces.

Histologically, the luminal portion of the mucosa is covered with surface epithelium, the cardia contains cardiac glands, the body including the fundus harbors gastric glands and the pylorus is lined with pyloric glands. The *surface epithelium* is tall columnar and discloses supranuclear mucus or mucinogen granules or, when these

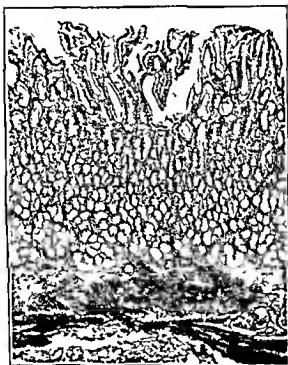


FIG. 257.—Normal stomach at the pylorus. $\times 375$

are not preserved, clear and transparent cytoplasm. A Golgi apparatus is also located in this area, while threadlike mitochondria are found in the basilar portion. Regeneration of cells takes place in the deeper portions of the pits. *Cardiac glands* are compound, tubular and open directly into the pits. They are lined with regular columnar epithelium that contains mucus. *Gastric glands* are simple branched tubules that penetrate the entire mucosa and that are arranged at right angles to the surface. They contain the following four types of cells: (1) Chief or zymogen which are arranged in a single row along the basement membrane and in the fasting state contain brilliant pepsinogen granules. (2) Parietal cells which are dispersed singly between the chief cells. They are more numerous towards the neck, are round or triangular, stain red with eosin, and

Chapter X

STOMACH

EMBRYOLOGY

THE stomach is first recognizable in the 4 mm. embryo as a somewhat flattened spindle-shaped enlargement of the foregut that rests within the thoracic cavity. With the relatively rapid growth of the head in the sixth and seventh weeks of embryonic life, however, it is gradually left behind to occupy its ultimate position in the upper portion of the abdomen. Simultaneously, the organ increases in length; its dorsal border grows faster than its ventral one resulting respectively in the greater and lesser curvatures; the fundus bulges from its cephalic portion; the dorsal mesentery grows more rapidly than the ventral one; it rotates so that the greater curvature points to the left, the lesser curvature to the right, the right surface dorsally and the left surface ventrally, and the cephalic end is pushed to the left by the growth of the liver. The gastric mucosa comes from the original entoderm whereas the connective tissue, muscle and peritoneum arise from the splanchnic mesoderm.

ANATOMY

Although the *shape* and *position* of the stomach varies according to the amount of its contents, its digestive stage and the condition of the intestine, when one is in the erect posture, it is roughly J-shaped, and it occupies the umbilical, epigastric and left hypochondriac portions of the abdomen. Its opening into the esophagus is called the *cardiac orifice* and is situated to the left of the midline opposite the eleventh dorsal vertebra, while its opening into the duodenum is known as the *pyloric orifice* and is located 1.5 cm. to the right of the midline opposite the first lumbar vertebra. The *lesser curvature* crosses the right crus of the diaphragm, forms a dip near its caudal portion that is called the *incisura angularis*, and gives attachment to the hepato-gastric ligament. The *greater curvature* is about five times the length of the lesser, and gives attachment to the gastro-splenic ligament and the greater omentum. There are two *surfaces*—an antero-superior which lies under the left costal margin, diaphragm, left and quadrate lobes of the liver and anterior abdominal wall, and a postero-inferior which covers the diaphragm, part of the spleen, left adrenal, upper pole of the left kidney, pancreas, left colic flexure and upper portion of the transverse meso-colon. The stomach is divided into a large left portion known as the *body* and a small right portion known as the *pylorus* by a transverse line drawn from the incisura angularis. The *cardia* is the portion of the body at the entrance of the esophagus and the fundus is the bulge to the left of the cardia. The *pyloric antrum*, or simply antrum as it is usually called, is that portion of the pylorus that

folds of redundant mucosa. *Histologically*, there is both a hypertrophy and hyperplasia of the circular layer of smooth muscle together with edema and leukocytic infiltration of the submucosa (Fig 258). The *diagnosis* is made from (1) a history of progressive vomiting often in a first born male infant that starts two weeks after birth, (2) visible gastric peristalsis and (3) a palpable pyloric tumor. It is confirmed in doubtful cases by roentgenographic study of ingested barium. The lesion must be differentiated from pyloro-spasm, intracranial injury, organic obstructions in other portions of the intestinal tract, and improper feeding. *Treatment* consists of



FIG 258—Hypertrophic pyloric stenosis after operation. The hypertrophied circular muscle layer has been severed. There is edema and leukocytic infiltration of the submucosa. $\times 2$.

surgically incising the musculature down to the submucosa, thereby releasing the sphincteric action. *Complications* which may arise are perforation of the mucosa, otitis media, wound infection and pneumonia. The over all *prognosis* is good. The mortality should not exceed 2 per cent.

Diaphragmatic hernia is a protrusion of the stomach or other abdominal viscera through a normal or an abnormal opening in the diaphragm. In some cases, the cause is an obvious congenital anomaly such as a short esophagus or a failure of the diaphragm to develop properly. In others, there is merely an inherited weakness which is aggravated by age, obesity, stretching of the esophageal hiatus from insufficiency of the muscle, decrease of tissue in esopha-

disclose intracellular canaliculi. (3) Mucous neck cells. These are located in the neck of the glands and are interspersed between the parietal cells. (4) Argentaffine cells. They are single, are located between the basement membrane and chief cells, and take a positive stain with silver salts. *Pyloric glands* have deeper pits and are of the simple, branched, coiled, tubular type (Fig. 257). The cells contain pale somewhat granular cytoplasm with a flattened basilar nucleus and resemble both the mucous neck glands and Brunner's glands of the duodenum. The remaining coats of the stomach consist of a tunica propria which contains lymphoid tissue, a muscularis mucosa, a submucosa containing neutrophils, eosinophils, lymphocytes and monocytes, and a muscle coat composed of an inner oblique, a middle circular and an outer longitudinal layer.

PATHOLOGY

Congenital Anomalies.—Development malformations of the stomach consist of: *failure to descend* into the abdomen resulting in a thoracic stomach or diaphragmatic hernia, maintenance of the *antero-posterior fetal position*, *reversion of rotation* as is seen in situs inversus, *atresia* or *stenosis* of the pyloric or cardiac orifice, *diverticula*, *absence of the cardia*, *failure of the musculature* to cover the entire surface and the presence of *aberrant tissue* such as the pancreas. The only three of the foregoing that need be considered further are hypertrophic pyloric stenosis, diaphragmatic hernia and diverticula.

Hypertrophic pyloric stenosis has been described both in adults and in infants. In the former it may be congenital or it may be acquired, but in either case it is rare, while in infants it is always developmental in origin and is common. The lesion is an enlargement of the pyloric muscle and evolves from an attempt of this portion of the stomach to overcome a spastic and resistant pyloric sphincter. The occlusion is rendered more or less complete by mucosal and submucosal edema which is consequent to mechanical irritation of food. The condition has a hereditary tendency as evidenced by its occurrence in identical twins and successive generations, affects males in 85 per cent of the cases, and is found in the first born infant in about two-thirds of the cases. *Symptoms* become manifest in from two to five weeks after birth. At first, they consist of regurgitation at infrequent intervals, but later, there is explosive vomiting after almost every meal. Because of the loss of food, fluids and electrolytes, there is failure to gain and later, actual loss of weight, dehydration, alkalosis and scanty stools. Examination after feeding discloses peristaltic gastric waves, and after vomiting a small tumor mass in the region of the pylorus. Ingestion of a thin barium mixture reveals gastric dilatation, a constriction and elongation of the pylorus, intermittent contractions and retention of at least three-quarters of the barium at the end of three hours.

Grossly, the pylorus is converted into a pale, hard, cylindrical mass that measures about 3 cm. in length and 1.5 cm. in diameter. Its proximal portion tapers off in the gastric wall, whereas its distal part ends abruptly. Cross section discloses a lumen occluded by

geal ring, increase of intra-abdominal pressure and trauma. The incidence of diaphragmatic hernia is reported as 0.75 to 2.1 per cent of all gastro-intestinal examinations. The lesion is discovered at all ages, with a preponderance in middle life. *Symptoms*, when present, depend upon the amount of mechanical interference with function of the herniated viscus, the degree of diaphragmatic dysfunction and the amount of increased intrathoracic pressure. Accordingly, they are extremely protean and may simulate gastric ulcer, coronary occlusion, cardiospasm, intestinal obstruction or cholelithiasis.

The *size* of the *opening* varies from several centimeters to that occupying most of the diaphragm, although the majority are less than 7 cm. in diameter. In about two-thirds of all cases, the defect is around the esophagus, whereas in most of the rest, it is in the posterior or postero-lateral portion of the diaphragm and in a few, it is anteriorly behind the sternum or through the central portion. A hernial sac covers all of the esophageal hiatal hernias, and about 10 per cent of the posterior and postero-lateral ones. The viscus herniated usually consists of the stomach, intestines or spleen. If it protrudes into the mediastinum, it may produce pressure upon the heart, whereas if it extends into the pleural cavity it causes collapse of the ipsilateral lung, a shift of the heart and mediastinum to the opposite side and compression of the opposite lung. The stomach may disclose an hour glass constriction depending upon the size of the hernial ring and the mucosa opposite the compression may be ulcerated. The latter is frequently the cause of bleeding which over a long period may be of sufficient magnitude to result in anemia. Other *complications* which have been described are obstruction and carcinoma.

The *diagnosis* is usually made roentgenographically from either an ordinary film which discloses the air bubble above the diaphragm, or from a film in which barium has been used to outline the herniated portion of the stomach and the constriction. Measurement with an esophagoscope will disclose a short esophagus in cases where this abnormality is a factor, and ulceration of the mucosa opposite the constriction when this complication is present. A differential diagnosis includes almost any pathologic condition in any of the organs in the upper abdomen. When there are no accompanying symptoms, *treatment* is unnecessary. Otherwise, medical therapy in the form of a bland diet, alkalies and antispasmodics is worthy of trial. If this fails, surgical interruption of the phrenic nerve or repair of the diaphragmatic defect is indicated. The ultimate *prognosis* is usually favorable.

Diverticula of the stomach are relatively uncommon. Although figures as to their incidence vary greatly, it has been stated that they constitute approximately 0.65 per cent of all gastric lesions, 0.11 per cent of all necropsies and 0.09 per cent of all laparotomies. They are ordinarily divided into (1) *congenital* where all the layers of the stomach are present and (2) *acquired* which are herniations of the gastric mucosa through the muscle coats. The former are caused by an arrested or faulty development in fetal life, whereas

emia. *Histologically*, the epithelium may be intact or it may show superficial erosions. The epithelial cells show an increase of mucus in their supranuclear portions with granularity of the subnuclear cytoplasm or the entire cells may be distended with mucus and the nucleus flattened and pushed against the basement membrane. The immediately underlying connective tissue discloses edema, fibrin, engorged capillaries, plasma cells, erythrocytes and neutrophils. *Chronic atrophic gastritis* may show a normal mucosa or one that is diffusely or focally replaced with a flat, glistening, smooth transparent lining through which the submucosal capillary network can be visualized. *Histologically*, the surface epithelium is transformed into an intestinal type disclosing an absence of mucus, a cuticular border along the free border, numerous goblet cells and Paneth cells at the bottom of the crypts. Sometimes, there is a proliferation of these altered cells to form intraluminal adenomatous buds. At other times, isolated groups of parietal cells from the original epithelium may be dislocated in the underlying connective tissue. Other epithelial changes that occur, are a transformation of the body glands into pyloric type of mucous glands and occlusions of some of the glands to produce cysts. In the subepithelial connective tissue, there is an increase of collagen and an infiltration with plasma cells and lymphocytes. The latter may form definite follicles and are not only confined to the submucosa but may infiltrate between the muscle coats to the serosa. *Chronic hypertrophic gastritis* may also be focal or diffuse. It is characterized grossly by a threefold or more increase in thickness of the mucosa with a conspicuous increase of the depths of the furrows and a corresponding prominence of the rugae (Fig 260). The epithelium shows marked adenomatous hyperplasia and the pits become elongated and cork-screw-like (Fig 261). Sometimes, they form deep lying cysts. The surface cells are tall, or rarely flat, their borders are indistinct, the mucus is reduced or missing, there are vacuoles between the cells, and the nuclei are irregular in position, and large and oval or thin and pyknotic. The underlying stroma discloses edema, fibrosis and an infiltration with plasma cells, macrophages and neutrophils.

The clinical diagnosis is made radiologically and gastroscopically. The latter discloses the appearance of the mucosa as already outlined and the former reveals a disturbance in motility, and changes in the mucosal pattern. A differential diagnosis includes gastric ulcer and carcinoma. Treatment is medical, although the hypertrophic type of inflammation is often resected surgically under a mistaken diagnosis of carcinoma. Concerning complications of chronic gastritis, there is evidence that the lesion may be followed by chronic ulcer, but that it is a precursor of carcinoma is still debated. The prognosis regarding longevity is favorable.

Gastric ulcer is usually considered in conjunction with duodenal ulcer under the designation of peptic ulcer. While the two lesions do have many factors in common they also have some differences and it is, therefore, deemed advisable to describe them separately.

Numerous theories have been promulgated to explain the cause of gastric ulcer, but none has been entirely satisfactory. From the

biotic and chemotherapy. When the phlegmon has localized surgical drainage, resection or marsupialization is indicated. One *complication* that is said to occur in one-half of the cases is peritonitis. The *prognosis* is guarded for the mortality rate is reported as high as 80 per cent.

Chronic gastritis is said to occur in about 3 per cent of the general population. The *cause* is not definitely known although the following are considered to play an etiological rôle: (1) capillary hemorrhage with incomplete healing of the resultant necrosis, (2) repeated injuries to the gastric mucosa from blood borne toxins and infections, (3) avitaminosis, (4) allergy and (5) hostility and anxiety states.

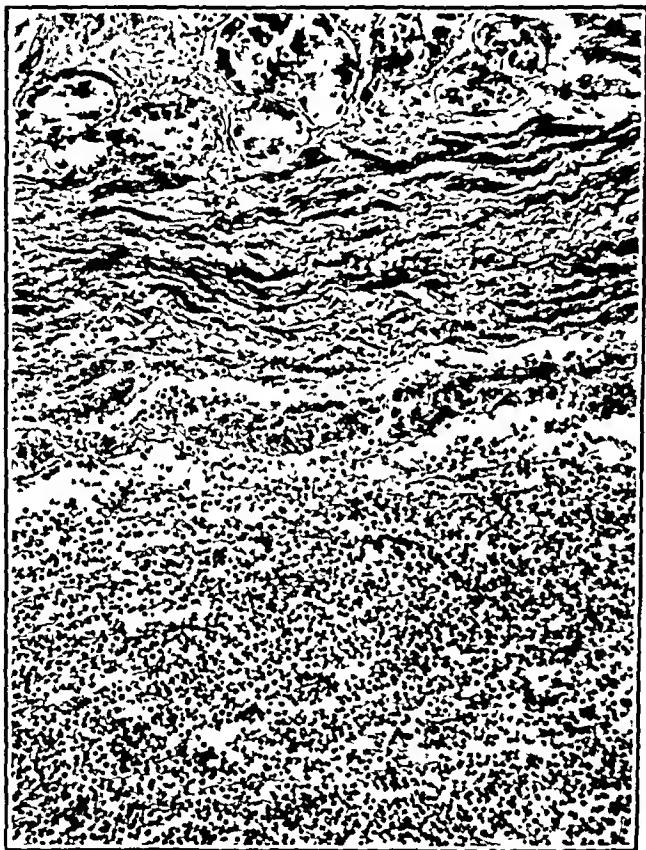


FIG. 259 — Acute phlegmonous gastritis showing edema of the submucosa and a massive infiltration with neutrophils x 50.

The latter produces hyperemia of the mucosa which renders the epithelium more susceptible to injury and the resultant erosions and inflammation are aggravated by a concomitant increase in acidity of the secretions. *Symptoms* are neither constant nor distinctive. Sometimes they are those of gastric ulcer, while at other times they simulate carcinoma. There may be epigastric distress which is or is not related to meals, poor appetite, weakness, fatigue, unexplainable nervousness, sore tongue, numbness and tingling of the extremities, hemorrhages, nausea and vomiting.

Pathologically, chronic gastritis is divided into three types—superficial, atrophic and hypertrophic. *Chronic superficial gastritis* discloses a thin layer of adherent mucus, edema and foci of hyper-

emia *Histologically*, the epithelium may be intact or it may show superficial erosions. The epithelial cells show an increase of mucus in their supranuclear portions with granularity of the subnuclear cytoplasm or the entire cells may be distended with mucus and the nucleus flattened and pushed against the basement membrane. The immediately underlying connective tissue discloses edema, fibrin, engorged capillaries, plasma cells, erythrocytes and neutrophils. *Chronic atrophic gastritis* may show a normal mucosa or one that is diffusely or focally replaced with a flat, glistening, smooth transparent lining through which the submucosal capillary network can be visualized. *Histologically*, the surface epithelium is transformed into an intestinal type disclosing an absence of mucus, a cuticular border along the free border, numerous goblet cells and Paneth cells at the bottom of the crypts. Sometimes, there is a proliferation of these altered cells to form intraluminal adenomatous buds. At other times, isolated groups of parietal cells from the original epithelium may be dislocated in the underlying connective tissue. Other epithelial changes that occur, are a transformation of the body glands into pyloric type of mucous glands and occlusions of some of the glands to produce cysts. In the subepithelial connective tissue, there is an increase of collagen and an infiltration with plasma cells and lymphocytes. The latter may form definite follicles and are not only confined to the submucosa but may infiltrate between the muscle coats to the serosa. *Chronic hypertrophic gastritis* may also be focal or diffuse. It is characterized grossly by a threefold or more increase in thickness of the mucosa with a conspicuous increase of the depths of the furrows and a corresponding prominence of the rugae (Fig 260). The epithelium shows marked adenomatous hyperplasia and the pits become elongated and cork-screw-like (Fig 261). Sometimes, they form deep lying cysts. The surface cells are tall, or rarely flat, their borders are indistinct, the mucus is reduced or missing, there are vacuoles between the cells, and the nuclei are irregular in position, and large and oval or thin and pyknotic. The underlying stroma discloses edema, fibrosis and an infiltration with plasma cells, macrophages and neutrophils.

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Numerous theories have been promulgated to explain the cause of gastric ulcer, but none has been entirely satisfactory. From the

maze of literature on the subject three facts, however, do emerge, (1) that there is a constitutional predisposition, (2) that the normal resistance of the mucosa is lost or, to put it another way, its vulnerability is increased and (3) that there is an absolute or at least a relative sustained increase of gastric juice—particularly of the acid and of the pepsin components. It has been known for centuries that certain *types of individuals* are more likely to develop ulcers than others. In physique, the ulcer susceptible are usually long and slender and have a delicate bony structure, narrow subcostal angles, narrow facies and accentuation of the feminine part of their



FIG. 260.

FIG. 261.

FIG. 260 —Chronic hypertrophic gastritis that simulated carcinoma. The furrows are deep and the rugae are prominent.

FIG. 261.—Chronic hypertrophic gastritis illustrating a portion of a furrow lined with greatly hyperplastic corkscrew-like glands. From the same case shown in figure 260. x 50.

make-up. They frequently show hyperactivity of the sympathetic nervous system in the form of sweating of the palms, wide palpebral fissures, slight sinus arrhythmia and slowing of the pulse by deep breathing or pressure upon the carotid sinus. Mentally, they are often above the average in intelligence, are high principled, emotional, exact and always striving for perfection. Despite this knowledge, however, it is also known that many such people never develop gastric ulcers, and so this constitutional type merely affords a fertile soil for other factors. One of these is a *loss of normal resistance* or an increased vulnerability of the mucosa. It has been suggested that this is brought about by avitaminosis, hypersensi-

tivity, deficiency of mucus which normally serves as a protective lining, micro-organisms and parasites, hypermotility of the stomach, cytotoxins, deficiency of anti-pepsin permitting autodigestion of the mucosa, vascular sclerosis thrombosis or spasm, capillary engorgement (either passive, such as occurs in shock or active, such as accompanies normal hypersecretion of gastric juice), and perhaps a deficiency of enterogastrone. Theoretically, enterogastrone is a substance produced by the mucosa of the intestines (in response to adequate fat and sugar in the chyme) which inhibits both gastric secretion and motility. Simultaneously, it appears to make the mucosa more resistant to ulceration. Although it has been said to have a salutary effect in experimentally produced ulcers in dogs, its beneficial effect in man still awaits confirmation.

The role of the third factor in the production of gastric ulcer, namely *gastric juice*, is explained as follows. It is known that pure gastric juice digests living tissue, and it is thought that gastric mucosa is normally resistant because the secretion is diluted by saliva, food, mucus and duodenal contents. It is obvious that hypersecretion of gastric juice has the same effect as lack of dilution. In experimental animals, it has been shown that a continued excess of gastric juice brought about either by stimulation of the vagus nerves or by subcutaneous implantation of histamine in beeswax will result in progressive peptic ulcerations. In man, it has been repeatedly demonstrated that the ulcer patient not only secretes more juice in response to a test meal, alcohol or histamine than does the normal, but also that the night acid secretion is considerably increased. The latter is the more important from the stand point of ulcer formation for it is not dependent on food, is inadequately diluted and is neurogenic in origin. Because of the latter, it is controlled by the autonomic nervous system, is, therefore, subject to psychic impulses coming from the brain by way of the vagus nerves, and is consequently closely associated with the ulcer susceptible individual described above. These contentions appear to be supported by recent preliminary studies on *vagotomized patients*. In such cases, it is stated that there is an immediate drop of free and total acid, a reduction of the total night secretion, an increase of pH of from one to three units over the previous level, and a decrease in gastric motility and tonus. It is further alleged that the net result of these changes is immediate and sustained alleviation of ulcer symptoms and a healing of the ulcers themselves. Within a year, however, the secretions, motility and tonus have been reported to return to normal, but because the pathway for psychic stimuli from the brain has been interrupted the night acid secretion remains low and the ulcers are said not to recur.

Gastric ulcer is about as frequent as duodenal ulcer, although clinically, it appears to be much less common because many of the acute lesions are not diagnosed. It affects males in about 88 per cent of all cases, is first apparent after the age of twenty years in approximately 90 per cent of the cases and is familial in 14 per cent of the cases. The chief *symptom* is epigastric discomfort or pain that is relieved by food. There may be tenderness in the epigas-

trium, vomiting after meals, hematemesis and melena or occult blood in the stools. The appetite is unaffected, and there is no loss of weight. Hyperchlorhydria is slightly more frequent than it is in normal individuals, and achlorhydria is present in about 6 per cent of the cases. It is characteristic of gastric ulcer for symptoms (1) to abate and disappear for long periods of time and (2) to exacerbate in the fall and spring of the year.

Pathologically, the first indication of a gastric ulcer is erosion of the mucosa. Erosions are located in any portion of the stomach and consist of shallow often hemorrhagic superficial saucer-shaped de-

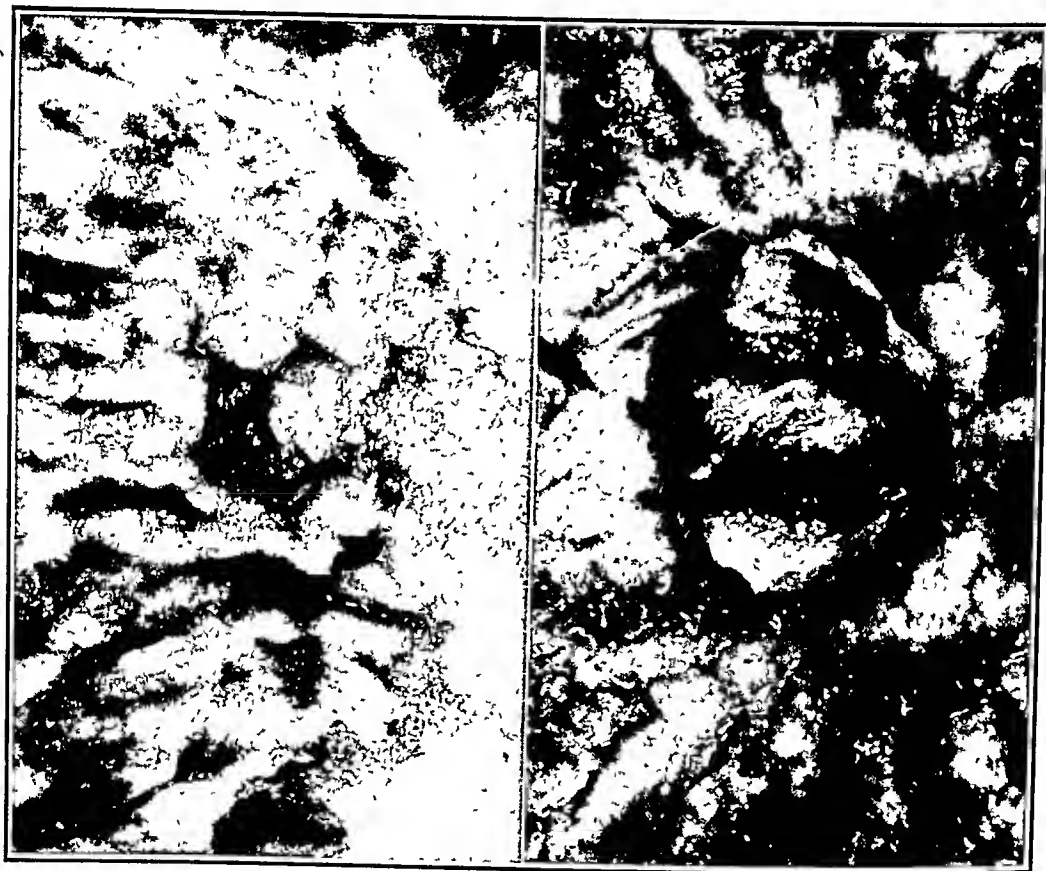


FIG. 262

FIG. 263.

FIG. 262.—Acute gastric ulcer. The borders are irregular and the edges are precipitous. (Heibut, Surgery Gynecology & Obstetrics)

FIG. 263 —Chronic gastric ulcer showing a flat border and undermined edges.

pressions that penetrate the mucosa for varying depths and that measure as much as 6 mm. in diameter. By the time they penetrate to the submucosa, they are associated with an inflammatory reaction and are, therefore, considered as acute ulcers. The latter have the same distribution as do the erosions; they penetrate the wall to varying depths sometimes to include the serosa, and they measure in size from a few millimeters to 1 or 2 cm. (Fig. 262). The outlines are irregular but sharp; the edges are steep and often undermined; the floor is covered with necrotic material or is clean, and the base is composed of thick and edematous submucosa, muscle or serosa. Most of the erosions and many of the acute ulcers heal

completely and are never recognized clinically. Evidence for this is gleaned from the fact that although these acute lesions doubtlessly precede benign *chronic* ulcers, the latter have a limited distribution. They are most frequently found along the lesser curvature and in the midportion of the posterior, and to a lesser degree the anterior wall of the stomach. As a rule, they measure 1 to 2 cm in diameter, although some are more than 4 cm across (Fig 263). They are oval or round and have a smooth, flat and less often a raised border. The edges are funnel-shaped, descend in the form of steps, or are undermined. The floor is clean and the base, composed of the



FIG 264

FIG 265

FIG 264—Gastric erosion—the first stage in the formation of an acute gastric ulcer. From case illustrated in Fig 262. $\times 37.5$

FIG 265—Another area from the case illustrated in figure 262 showing progression of the lesion to form an acute ulcer. $\times 37.5$

muscle layers or the serosa, is grey and firm. When viewed from the serosal surface, the center of the ulcer is grey or white and sometimes puckered with the periphery of this patch gradually fading into the normally pink surrounding serosa. Histologically, erosions consist merely of a denudation of the mucosal cells to various depths (Fig 264). As the process penetrates deeper, and particularly when it involves the submucosa, it then becomes an acute ulcer (Fig 265). As such the epithelium is completely lost, and usually undermined. The floor and base from within out consist of an inner zone of necrosis and fibrin, an intermediate zone of neutrophils and nuclear fragments, and an outer zone of granulation tissue which consists of fibroblasts, capillaries, neutrophils, plasma

trium, vomiting after meals, hematemesis and melena or occult blood in the stools. The appetite is unaffected, and there is no loss of weight. Hyperchlorhydria is slightly more frequent than it is in normal individuals, and achlorhydria is present in about 6 per cent of the cases. It is characteristic of gastric ulcer for symptoms (1) to abate and disappear for long periods of time and (2) to exacerbate in the fall and spring of the year.

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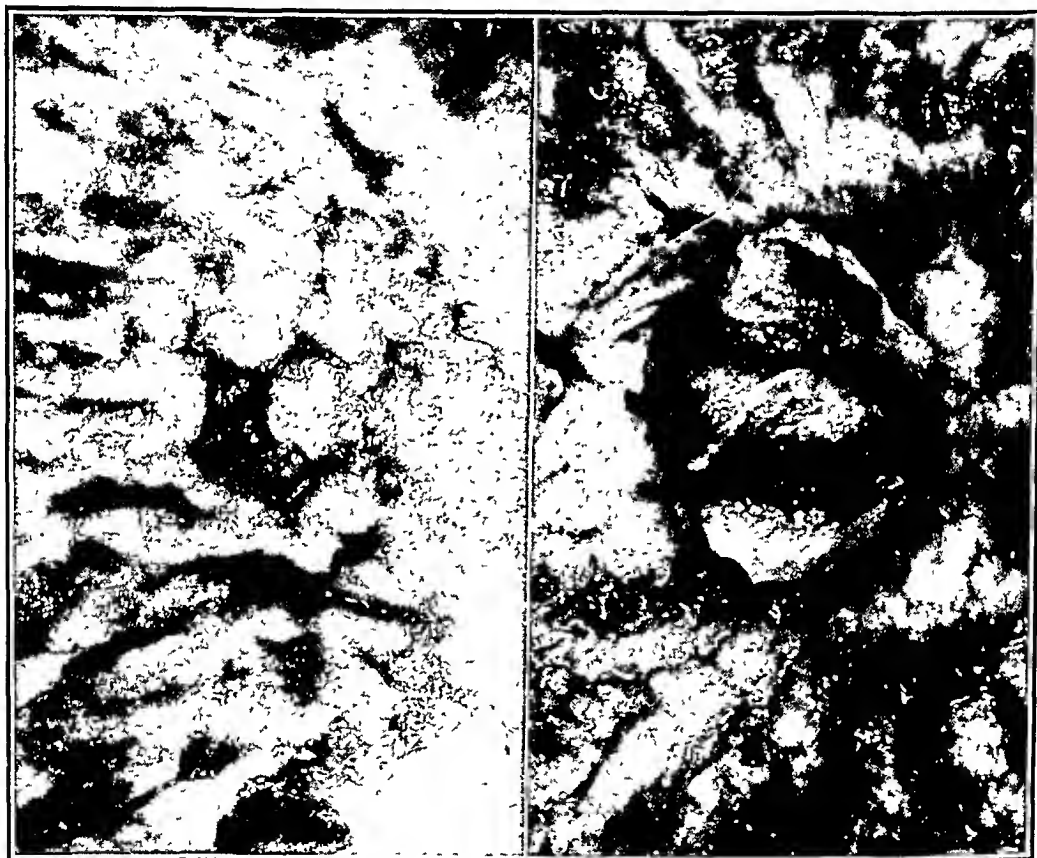


FIG 262.

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Perforation occurs in 11 per cent of all gastric ulcers that do not heal. It predominates in males, occurs at any age and in any season, has no predilection for any particular occupation and is brought about by the same factors that cause the initial ulceration, but is often precipitated by trauma following a heavy meal. The usual site of perforation is the anterior wall at the lesser curvature near the pylorus. The perforation is, as a rule, into the peritoneal cavity, but if the lesion is located opposite other organs, it may penetrate into the pancreas, gall bladder, liver, diaphragm and extrahepatic bile ducts. The opening measures as much as 1 cm in diameter, the adjacent serosa has a dull appearance, and there is a varying amount of surrounding exudate. The resulting peritonitis is first chemical and later bacterial. *Symptoms and signs* of perforation are sudden pain, prostration, abdominal rigidity, air in the peritoneal cavity, nausea and vomiting, and leukocytosis to 35,000 per cubic millimeter. *Treatment* is surgical closure of the perforation. If operated upon within the first six hours, the mortality is 10 per cent, if after twenty-four hours, it is 62 per cent. The mortality rate is greater in women than it is in men, and it increases with advancing years. In general, three-quarters of the patients should recover.

Stenosis results from contraction of fibrous tissue which is an expression of repair. If the lesion is at the pylorus, a moderate degree of fibrosis will result in occlusion. If it is in the midportion of the stomach and the lesser curvature, it will constrict the organ to produce an hour-glass type of deformity. *Symptoms* are those of obstruction. The *treatment* is operative.

Carcinomatous transformation of a chronic gastric ulcer has been estimated to occur from 0 per cent to 68 per cent of all cases. It is probable that the truth lies in the neighborhood of 6 per cent. There is no question that many lesions are treated as benign ulcers only to find that the patients later have gastric carcinoma, but whether these are ulcers that have become cancerous or cancers that are ulcerating it is often impossible to tell. *Clinically*, some ulcerating carcinomas respond to medical therapy in a manner identical to that of benign ulcers, in that symptoms disappear and the crater fills in by granulation tissue or cancer cells, leaving it no longer demonstrable roentgenographically. Nor can one draw hard and fast rules from the location and size of the ulcer. In general, however, it may be said that any ulcer within 2 cm of the pylorus is prone to be malignant, that nearly all ulcers on the greater curvature and in the fundus are cancerous, that 20 per cent of those on the anterior and posterior wall are carcinomatous and that many ulcers over 3 cm in diameter are neoplastic. *Histologically*, it is said (1) that the base in ulcerating carcinoma always contains continuous bands of muscle whereas in ulcer that has become cancerous the muscle coat is always breached and its ends are turned towards the mucosa, (2) that in ulcers becoming cancerous there are large areas of collagenous fibrous tissue in the base that are not penetrated by neoplastic cells. Such areas are not found in ulcerating carcinomas, and (3) that obliterative endarteritis and thrombophlebitis are

cells, lymphocytes and macrophages. The inflammatory cells penetrate the surrounding structures in all directions and as vessels are encompassed, there develop both an obliterative endarteritis and a thrombophlebitis. When the ulcer becomes more apparent and when it becomes chronic, collagenous fibrous tissue becomes more abundant and the leukocytic infiltration wanes. When finally the ulcer heals, the entire defect is completely replaced with a contracted depressed grey scar.

If healing does not occur, the ulcer may persist or it may result in one of four *complications*; (1) massive hemorrhage, (2) perforation, (3) stenosis and (4) a carcinomatous transformation.

Massive hemorrhage from gastric ulcer usually occurs when the lesion involves the lesser curvature and is, therefore, the result of erosion of the right or left gastric arteries or their branches (Fig 266).



FIG. 266 —Eroded vessel at the base of an acute gastric ulcer causing massive hemorrhage and death of the patient x 37 5. (Herbut, Surgery Gynecology & Obstetrics).

Nineteen per cent of all ulcers that do not heal will in time be complicated by hemorrhage. Its seriousness lies in the frequent fatal outcome. The first *indication* of hemorrhage may be profound shock, hematemesis or the passage of blood by rectum. Hemorrhages that may prove fatal are those in which the patient fails to improve promptly under the following treatment; (1) strict bed rest, (2) moderate morphine, (3) withholding all food by mouth, (4) adequate blood transfusions and (5) recurrent hemorrhages when the patient is on a strict régime. *Treatment* is medical if the patient is under forty-five years of age and bleeding for the first time. It is surgical if he is over forty-five years of age, if hemorrhages have been repeated and if he has failed in the past to respond to medical therapy. If treated surgically before forty-eight hours, the mortality is 10 per cent, if after forty-eight hours, it is 70 per cent.

Perforation occurs in 11 per cent of all gastric ulcers that do not heal. It predominates in males, occurs at any age and in any season, has no predilection for any particular occupation and is brought about by the same factors that cause the initial ulceration, but is often precipitated by trauma following a heavy meal. The usual site of perforation is the anterior wall at the lesser curvature near the pylorus. The perforation is, as a rule, into the peritoneal cavity, but if the lesion is located opposite other organs, it may penetrate into the pancreas, gall bladder, liver, diaphragm and extrahepatic bile ducts. The opening measures as much as 1 cm in diameter, the adjacent serosa has a dull appearance, and there is a varying amount of surrounding exudate. The resulting peritonitis is first chemical and later bacterial. *Symptoms and signs* of perforation are sudden pain, prostration, abdominal rigidity, air in the peritoneal cavity, nausea and vomiting, and leukocytosis to 35,000 per cubic millimeter. *Treatment* is surgical closure of the perforation. If operated upon within the first six hours, the mortality is 10 per cent, if after twenty-four hours, it is 62 per cent. The mortality rate is greater in women than it is in men, and it increases with advancing years. In general, three-quarters of the patients should recover.

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found in ulcers that have become malignant but are not present in ulcerating cancers.

The *diagnosis* of *gastric ulcer* is made by obtaining a history of epigastric pain relieved by food, by demonstrating the crater radiologically and by visualizing the defect gastroscopically. *Treatment* is not standardized. Medical therapy (consisting of a bland diet, antispasmodics, sedatives and antiacids) gives temporary success in about 80 per cent of the cases, but permanent cures are effected in less than 50 per cent. Specific indications for operation are obstruction, perforation, hemorrhage, intractable pain and failure of healing of the defect within three weeks when the patient is on a medical régime. In view of the inability, however, to distinguish between an ulcerating carcinoma and a benign ulcer, the current trend is to treat all gastric ulcers surgically. Although there are several operations in vogue, it appears that the most satisfactory procedure is to remove the ulcer, the lesser curvature and three-quarters of the stomach including the antrum, and to perform the anastomosis such that the jejunal loop is as short as possible. Any anastomosis between the stomach and jejunum carries with it a 2 to 10 per cent danger of a *stomal ulcer*. The causes of the latter are the same as those of the original ulcer; it occurs at any age; it is more common in men than in women, and it may appear in from forty-eight hours to many years after the operation. The most outstanding *symptoms* are pain, hemorrhage and vomiting. The *location* of the ulcer is on the jejunal side in 81 per cent of the cases, gastric side in 3 per cent and at the line of anastomosis in 16 per cent. *Grossly*, the ulcer is round or oval, sharply demarcated, clean and penetrates the wall to varying depths. In some cases, it perforates the colon to produce a gastrojejuno-colic fistula. The *histopathologic* changes are similar to those seen in gastric ulcer. Because of the numerous factors involved, no precise statement can be made regarding the *prognosis* in gastric ulcer. In general, it may be said that acute ulcers usually heal, that less than 50 per cent of the remainder are cured by medical treatment, that symptoms are alleviated in 100 per cent of the cases treated surgically, and that the operative mortality should not exceed 5 per cent.

Specific Inflammations.—Granulomatous inflammations of the stomach consist of *Boeck's sarcoid*, *actinomycosis*, *syphilis* and *tuberculosis*. Only the latter two are frequent enough to merit separate consideration.

Syphilis of the stomach is confined to the *tertiary* type. It usually affects young adults, has no predilection for either sex, and is found in both the white and colored races. *Symptoms* and *signs* are not specific. They consist of epigastric pain, loss of weight, vomiting, anemia, achlorhydria, a positive serologic test for syphilis, stigmata of syphilis elsewhere and, occasionally, a palpable epigastric mass. Roentgenographically, there is a smooth funnel-shaped deformity of the pylorus and gastroscopically, one may see a contracted stomach with a pale mucosa.

The *lesion* involves the pylorus in 86 per cent of the cases, and in most of the remaining cases, it is located in the mid-portion of the

stomach In the former, it produces a more or less funnel shaped deformity whereas in the latter, it tends to produce an hour-glass like constriction. *Grossly*, the infection primarily involves the submucosa whence it spreads to the other layers in varying degrees. The size of the lesion varies but usually it measures about 4 to 6 cm across. The wall is thick, boggy, edematous, hyperemic and at first pliable but later rather tough. Mucosal ulcerations are secondary and are, therefore, usually saucer shaped and superficial. *Histologically*, there is as a rule a diffuse and perivascular infiltration with lymphocytes and plasma cells, although sometimes there are gummatoid foci composed of epithelioid cells with occasional peripheral giant cells. Two vascular lesions already considered in Chapter I are proliferative endarteritis and *panphlebitis*, or the so called *perivascularitis*. The latter is an infiltration of the veins



FIG. 267—Syphilitic perivascularitis. Elastic tissue stain. $\times 100$

from without with syphilitic granulation tissue resulting in their complete destruction and obliteration (Fig 267). When these changes are advanced the remnants of the vessels can be recognized only by elastic tissue stains.

The *diagnosis* is based upon the history, a positive serologic test for syphilis, gastric deformity seen radiologically and regression of the lesion under antisyphilitic therapy. It is confirmed histologically and by isolation of the *spirochetes* from rabbits testicles which have been previously injected with macerated tissue from the suspected lesion. *Treatment* is medical when the infiltration is seen early and when it produces no obstruction. When, however, there is hemorrhage, obstruction, pain or loss of weight or when the lesion is extensive, treatment consists of surgical excision. The *prognosis* is good.

Tuberculosis of the stomach has been reported as occurring in from 1 in 40 to 1 in 6000 tubercular adults and in from 1 in 7 to 1

in 200 tubercular children coming to necropsy. It has been postulated that the stomach ordinarily escapes infection because of the acid gastric juice, paucity of lymphatics, intact epithelium and rapidity of emptying. Gastric lesions are almost always associated with tuberculosis elsewhere in the body, and particularly with pulmonary infection. Tubercle bacilli gain entrance by way of the blood stream, lymphatics or contiguity from lymph nodes, spleen, gall bladder or pancreas. Penetration of the mucosa from the lumen probably does not occur. The disease is found at all ages and is said to involve males somewhat more frequently than females. The most common *symptoms* are vomiting, emaciation and diarrhea. The *lesions* are equally distributed between the pylorus and the body, and in about 90 per cent of the cases consist of single or multiple typical undermined ulcers of varying sizes. The remaining 10 per cent consist of miliary or conglomerate tubercles or of the hyperplastic and hypertrophic type of infiltration. *Histologically*, the characteristic unit is the tubercle. The tubercle bacillus has been isolated in only about one-quarter of all reported cases. A correct clinical *diagnosis* is seldom if ever made, for while a mucosal defect may be detected roentgenographically and gastroscopically, it can not be distinguished from an ordinary ulcer. *Treatment* consists of attention to the disease in other organs, which is usually more serious. The *prognosis* is poor.

Tumors.—From a histogenetic point of view, neoplasms of the stomach may be classified as follows: from the epithelium there may arise a papilloma, adenoma, cyst and carcinoma; from connective tissue a fibroma, myxoma, fibrosarcoma, and myxosarcoma; from vessels a hemangioma, lymphangioma and a hemangiosarcoma; from fat a lipoma and liposarcoma; from nerves a neurofibroma and neurofibrosarcoma; from muscle a leiomyoma and a leiomyosarcoma; from lymphoid tissue (reticulum cells) a lymphosarcoma, Hodgkin's disease and reticulum cell sarcoma; from mesodermal elements as a result of metaplasia an osteoma, and from misplaced embryonal buds a hamartoma. The most important of the benign lesions are papilloma, adenoma and leiomyoma, and of the malignant lesions carcinoma, leiomyosarcoma and the lymphoblastomas (lymphoid tumors).

Papilloma and Adenoma.—The terminology regarding these types of tumors is still used rather loosely. The term *papilloma* should be restricted to non-malignant tumors composed of epithelial cells covering branching stalks of connective tissue, while *adenoma* should be confined to tumors composed of epithelial cells in glandular formation supported by a scanty stroma of loose connective tissue. The term *polyp* signifies any tumor, epithelial or mesodermal, that is pedunculated and that arises from a mucosal surface. It is, therefore, non-specific and when used it should be further qualified. From these definitions, it is obvious that papilloma and adenoma are not only closely related, but that both are often found in a single specimen. The *distribution* in the stomach is as follows: one-quarter in the cardia, one-quarter in the body and one-half in the pylorus. In the latter they are equally distributed over the anterior

and posterior walls. They vary in diameter from a few millimeters to 3 or 4 cm, are flat excrescences or round masses, are attached by a sessile broad or narrow base and may be single or multiple (Fig 268). They are grey, brown or hemorrhagic and externally are granular, fissured or cystic. They may or may not be superficially ulcerated. *Histologically*, whether covering stalks or forming acini, the cells are never specialized but rather consist of cuboidal or columnar cells containing a moderate or large amount of mucus and round or oval deeply stained nuclei. Between the epithelial cells and in the underlying connective tissue there is an infiltration with lymphocytes, plasma cells and neutrophils. As a rule, the muscularis mucosa does not take part in the tumor but is stretched across the base and is intact or broken and frayed. These tumors are



FIG 268 — Adenomatous polyp of the stomach adjacent to a fungating carcinoma

more common in men than in women and usually occur after the age of thirty-five years. Many are asymptomatic until complications arise. The latter consist of (1) *ulceration* with repeated small or severe hemorrhages resulting in anemia, hematemesis or melena, (2) *pyloric obstruction*. If the tumor is at the pylorus, the mass itself plus the associated spasm produces the occlusion, while if the tumor is pedunculated, it occludes by becoming intussuscepted through the pylorus, (3) *malignant transformation* which is said to occur in from 35 to 80 per cent of all cases. The diagnosis is made (1) roentgenographically, wherein ingested barium discloses a punched out filling defect about which the rugae are nearly normal and (2) gastroscopically, by which means, of course, the tumor can be directly visualized. Treatment consists of surgical excision. The prognosis, before a cancerous change supervenes, is good.

Leiomyoma.—This tumor has been reported in as many as 46 per cent of all stomachs examined at necropsy and constitutes about 40 per cent of all benign gastric neoplasms. It is found in males as frequently as in females, and is either asymptomatic or produces symptoms similar to those of adenoma and papilloma. The sites of occurrence are at the pylorus 44 per cent, middle third 38 per cent, cardia 13 per cent and the remainder in other portions. The tumors usually arise from the inner muscular layer and, therefore, protrude beneath the mucosa in about 85 per cent of the cases. They are, as a rule, single but may be multiple, are sharply circumscribed grey and firm, and ordinarily do not measure more than 4 cm. in diameter. *Histologically*, they are composed of intertwining bundles of spindle cells with a moderate or an abundant amount of collagen and elongated deeply stained nuclei. Most of the tumors disclose inflammation, hyaline degeneration, fibrosis, calcification or liquefaction, and they may eventuate in volvulus, intussusception or a *sarcomatous transformation*. The latter is reported as occurring in from one-third to three-quarters of all cases. The *diagnosis, treatment and prognosis* are the same as in adenoma and papilloma.

Carcinoma.—Cancer of the stomach accounts for 38,000 deaths in the United States annually. It is, therefore, one of the most common and most serious of all diseases. Its cause or *causes* are not known despite the fact that the following are often listed as being of etiologic significance: (1) *heredity*, (2) *endocrine* disturbances, for it is known that hyperthyroidism produces hypochlorhydria or achlorhydria, that posterior pituitary hormone when injected into animals brings about ulcerations of gastric mucosa, and that parathyroid extract decreases the volume and acidity of gastric secretions, (3) *neurological* disturbances from the central nervous system, since lesions of the midbrain are known to co-exist with gastric ulcers, (4) variations in *gastric secretions*, as evidenced in part by the frequent occurrence of achlorhydria in conjunction with cancer, (5) *diet*, among which are hot food, alcohol, protein deficiency and prolonged inanition. Fasting and inanition will eventuate in gastric polyps in rats, and a protein deficient diet will produce ulcers in dogs, (6) action of *bacteria*, bacterial products and viruses and (7) action of unknown *carcinogens*. Dibenzanthracene and methylcholantrene have been used to produce adenocarcinoma of the stomach in mice. From the morphologic viewpoint gastric adenoma and papilloma are known to be *precancerous* lesions, carcinoma in situ is a pre-invasive type of cancer, chronic gastric ulcers develop into carcinoma in about 6 per cent of the cases and chronic gastritis associated or unassociated with pernicious anemia is considered by some to be a precursor to malignant epithelial tumors. In other words there is ample evidence to suggest that carcinoma of the stomach arises from a previously abnormal mucosa, but the causes of these changes are not known.

Clinically, carcinoma of the stomach is seen at all ages with a preponderance in the fifth and sixth decades and an average of about sixty years. It attacks males twice as frequently as females. Unfortunately, there are no clear cut or constant early *symptoms*. The

patient's complaints will depend upon the size and location of the tumor. Thus a nodule 5 mm in diameter that is situated at the pylorus may produce obstruction, whereas a mass 5 cm in diameter located in the mid-portion of the stomach may be entirely silent. Therefore, it should be the rule that any dyspepsia in a patient of middle age or beyond should be regarded as due to carcinoma until proved otherwise. Some of the more common complaints are chronic epigastric pains or aches or simply discomfort, weakness, fatigability, vomiting and loss of weight. Physical examination is not contributory in the early stages. The laboratory aids are a microcytic and less often a macrocytic type of anemia, occult blood in the stools and vomitus, and hypochlorhydria or achlorhydria in approximately two-thirds of the cases. Of indispensable value



FIG. 269.—Diffusely spreading carcinoma involving the pyloric portion of the stomach.

are (1) roentgenologic studies of a barium filled stomach which demonstrates decreased motility, a crater or a filling defect and (2) gastroscopic examination when many of the lesions can be visualized and some even biopsied.

Although carcinoma can arise in any portion of the stomach, about one-half of the lesions are located in the pyloric region. From both a macroscopic and microscopic point of view, numerous classifications have been advocated, but it appears that such subdivisions are more confusing than they are of real value (1) because the most significant fact is whether the tumor was completely excised or whether it had already metastasized rather than its gross or histologic appearance and (2) because there is so much overlapping of the different types that a precise cataloguing is frequently impossible. In the following description, therefore, adjectives will be for the most part omitted. Grossly, the carcinoma may fungate

into the lumen to produce a cauliflower-like mass; it may spread along the surface or along the various tissue planes of the stomach resulting in a diffuse thickening of the wall; it may penetrate and simultaneously ulcerate, or it may disclose combinations of these three manners of growth. *Fungating* cancers may or may not arise from previous adenomas or papillomas and, although usually single, they may be multiple (Fig. 268). Some are a few centimeters, while others are 6 cm. or more in greatest diameter. They are, as a rule, sessile, rarely pedunculated, moderately friable, superficially or deeply fissured, intact or slightly ulcerated, grey or greyish brown and are not, as a rule, firmly united with the deeper portions of the gastric wall. *Diffusely spreading* cancers may involve a portion of the stomach or the entire organ (Fig. 269). The carcinoma creeps along the surface and along the various planes to produce a uniform thickening that measures 1 to 3 cm. in depth.



FIG. 270.—Early ulcerating gastric carcinoma showing ill-defined margins and sloping edges.

Although most of the infiltration is in the submucosa, the neoplastic and overabundant fibrous tissue also penetrates between the muscle bundles and renders them conspicuous against the grey background. The mucosa is usually intact, but it may be superficially ulcerated; the lumen is moderately or greatly reduced, and the wall becomes firm and rigid. This type of growth is often referred to as *linitis plastica* or *leather bottle stomach*. *Penetrating* and *ulcerating* cancers are the most common. They are essentially of two types: (1) those that develop on the basis of a previous chronic ulcer and are grossly indistinguishable from the latter and (2) those that arise as carcinoma which ulcerates as it penetrates (Fig. 270). The latter lesions are of varying transverse diameters. The ulcerations are ordinarily round or oval, ill-defined or punched out, and initially shallow. The margins are often irregularly raised, firm and indurated for varying distances beyond the crater; the edge of the ulcer is sloping and often stepped; the floor is covered with necrotic material; the base is composed of cancer and fibrous tissue, and the

adjacent serosal surface is grey, puckered, scirred and granular. The remaining growths which are usually advanced lesions disclose combinations and variations of the aforementioned three basic patterns.

Histologically, cancer of the stomach varies considerably from tumor to tumor and from one area to another in the same tumor. Although squamous cell carcinoma or *carcinoma* has been described, it is so rare that most reports do not even mention it. For practical purposes a gastric carcinoma is an *adenocarcinoma* that at one extreme is well-differentiated and at the other is completely anaplastic. Basically, it is the mucous cell that becomes neoplastic.



FIG. 271

FIG. 272

FIG. 271 — Well differentiated adenocarcinoma of the stomach. $\times 50$

FIG. 272 — Mucinous carcinoma of the stomach showing scattered neoplastic cells in a sea of mucus. $\times 50$

In the well differentiated tumors, it forms rather regular acini that are lined with a single layer of columnar or cuboidal epithelium (Fig. 271). The cells are quite distinct, droplets of secretion are seen between the free border of the cell and the nucleus, and the nucleus located in the lower portion of the cell or adjacent to the basement membrane is round, oval or slightly irregular and hyperchromatic. In some cases, the mucus becomes over-abundant, fills large spaces, and encloses scattered single cells or clusters of cells (Fig. 272). This is the so-called *colloid*, *mucinous* or *gelatinous* carcinoma and, depending upon the amount of mucus, it may or may not be recognizable macroscopically. In still other cases, the mucus

into the lumen to produce a cauliflower-like mass; it may spread along the surface or along the various tissue planes of the stomach resulting in a diffuse thickening of the wall; it may penetrate and simultaneously ulcerate, or it may disclose combinations of these three manners of growth. *Fungating* cancers may or may not arise from previous adenomas or papillomas and, although usually single, they may be multiple (Fig. 268). Some are a few centimeters, while others are 6 cm. or more in greatest diameter. They are, as a rule, sessile, rarely pedunculated, moderately friable, superficially or deeply fissured, intact or slightly ulcerated, grey or greyish brown and are not, as a rule, firmly united with the deeper portions of the gastric wall. *Diffusely spreading* cancers may involve a portion of the stomach or the entire organ (Fig. 269). The carcinoma creeps along the surface and along the various planes to produce a uniform thickening that measures 1 to 3 cm. in depth.



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15 per cent of patients die from the carcinoma without any evidence of spread even at necropsy.

A diagnosis of cancer of the stomach should be suspected in any person past the age of forty years who has symptoms of indigestion. It is confirmed by roentgenologic studies, by gastroscopy and in some cases by gastroscopic biopsy. A differential diagnosis includes gastric ulcer, other tumors of the stomach both benign and malignant, and disease of the pancreas, liver, gall bladder and heart. The only effective treatment is surgical resection of the tumor. Whereas formerly the treatment of choice was partial gastrectomy, at the present time removal of the entire stomach regardless of the size of the cancer appears to be favored more and more. In either case, all the draining lymph nodes are removed. The ultimate disposition of any group of cases is approximately as follows (percentages are based on the entire group). Forty per cent are inoperable when first seen and 60 per cent are explored surgically. Following this an additional 22 per cent are found to be inoperable and roughly 25 per cent are apparently completely resectable. The operative mortality is about 16 per cent, thus leaving approximately 20 per cent that are given a chance of cure. At the end of five years only 5 per cent or less of the original number are alive. Aside from the presence of the tumor itself and its inherent dangers, two complications that sometimes occur are hemorrhage from erosion of a vessel and peritonitis from perforation of the ulcerating growth. The immediate complications following operation are peritonitis with or without leakage, pneumonia, shock from the extensive operative procedure, pulmonary embolism and mediastinitis.

Leiomyosarcoma—As the name implies this tumor arises from smooth muscle (directly or from a leiomyoma). It constitutes only about 10 per cent of all gastric sarcomas and the latter form approximately 4 per cent of all malignant tumors of the stomach. Leiomyosarcoma has no predilection for either sex and the average age is forty-nine years—about a decade less than carcinoma. Clinically, there are three cardinal manifestations: (1) gastrointestinal hemorrhage either severe or recurrent which results in anemia, (2) epigastric or left upper quadrant pain or discomfort and (3) an upper abdominal mass. Roentgenograms disclose a filling defect in 60 per cent of the cases which is frequently interpreted as an extrinsic mass. There may also be stiffness of the gastric wall and a mucosal ulcer. Gastroscopy may show a protruding mass which slopes gently to the surrounding mucosa. The tumor is primarily intramural, whence it may extend extragastrically, intraluminally or in both directions. It frequently reaches a diameter of 15 cm. It is firm, well-encapsulated or at least sharply demarcated, and when smaller diffusely greyish white. As it enlarges, it tends to become edematous, hemorrhagic, necrotic and even cystic. Sometimes the latter replaces most of the central portion of the mass leaving only a narrow rim of tumor tissue at the periphery. Calcification, hyaline degeneration, inflammation and abscess have also been recorded. Histologically, the tumor is composed of interlacing fusiform cells that are shorter, more rounded and somewhat less regular than

is retained within the epithelial cells producing sharply defined round bodies with vacuolated cytoplasm and peripherally compressed lunate nuclei (Fig. 273). This is the so-called *signet-ring cell carcinoma*. It is the type that is prone to metastasize to the ovaries to produce what has been called the *Krukenberg tumor*. At the opposite extreme is the *completely undifferentiated carcinoma* wherein the cells are arranged in clusters, strands, sheets or singly dispersed. They are frequently round or only slightly irregular, and may at first glance resemble reticulum cells or lymphoblasts. The cytoplasm is scanty or moderate in amount and the nuclei are round or somewhat oval and hyperchromatic (Fig. 273). Between these two extremes the *combinations* are many. In all carcinomas of the stomach there is an associated infiltration with varying

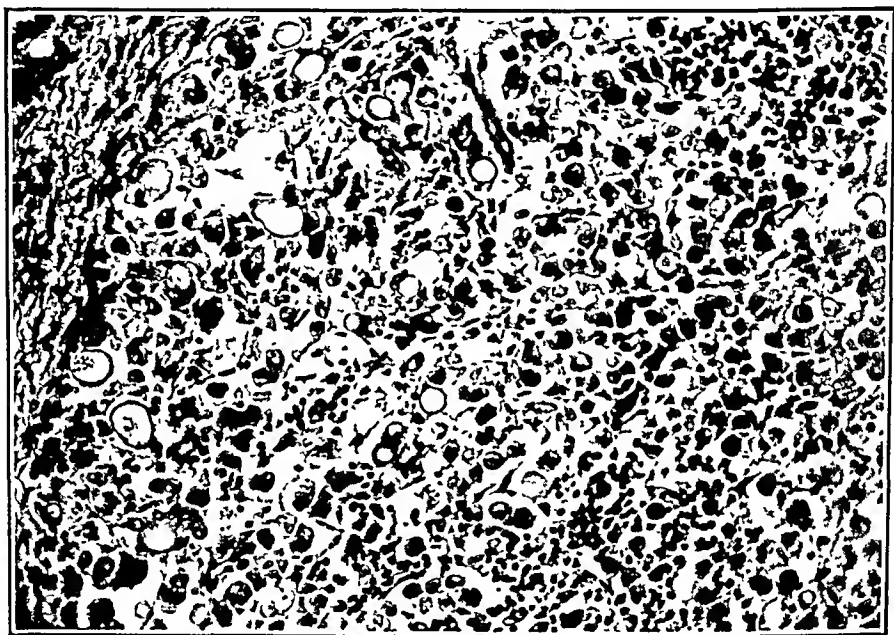


FIG. 273 —Anaplastic and "signet-ring" cell carcinoma of the stomach x 100

numbers of plasma cells, lymphocytes, monocytes, eosinophils and neutrophils. The degree of accompanying fibrosis is not uniform. In some cases, fibrous tissue formation is scanty, whereas in others, it is so profuse that the embedded neoplastic cells are found with difficulty and only after several sections are examined. The fibrosis reaches its acme in diffusely spreading cancers or the *linitis plastica* type of growth.

Carcinoma of the stomach *spreads* by (1) direct extension to the esophagus, duodenum, omentum, pancreas, colon, liver and diaphragm, (2) by lymphatic vessels to the nodes along the greater and lesser curvature, hilum of the liver, retroperitoneum and the left lower cervical region and (3) by the blood stream to the liver, peritoneum, lungs, ovaries, bones and all other organs of the body. Sometimes the primary lesion remains small and the secondary growths are many, large and widespread, whereas at other times the gastric lesion is large and confined to the stomach. About

15 per cent of patients die from the carcinoma without any evidence of spread even at necropsy.

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normal cells. The nuclei are similarly shaped, hyperchromatic and disclose numerous mitoses. The tumor expands into rather than infiltrates the neighboring tissues. Of the collected series, *metastases* to the liver, bones, lungs, and other organs occurred in 15 per cent of the cases. The *diagnosis* is usually not made until the abdomen is explored. *Treatment* is gastrectomy. The *prognosis* is better than in gastric carcinoma.

Lymphoblastomas.—Under this heading are included lymphosarcoma, reticulum cell sarcoma and Hodgkin's disease. While the former two each constitute about 30 per cent of all sarcomas of the stomach, Hodgkin's disease is responsible for only 8 per cent of these growths. Males are affected more frequently than females and the average age is about twelve years less than that in carcinoma. *Signs* and *symptoms* are not typical and consist of pain, belching, vomiting, anorexia, loss of weight and so forth. The *lesions* may involve only the stomach, or they may be part of a generalized systemic dissemination. They are more often found along the lesser curvature and posterior wall. They may be single or multiple, infiltrating or polypoid, superficially intact or ulcerated and vary in size from a few to many centimeters. They are soft or firm, and on section are diffusely grey or contain foci of necrosis and hemorrhage. *Histologically*, they resemble the respective lesions in lymph nodes and these are described in Chapter XVI. A *clinical diagnosis* is usually not possible. *Treatment* is gastrectomy followed by irradiation therapy. When the disease is localized to the stomach, the *prognosis* is better than it is in carcinoma, but when the gastric lesion is part of a systemic disease, the prognosis is poor.

Mechanical Disturbances.—Under this heading will be included gastrojejunocolic fistula, intussusception, volvulus, foreign bodies, obstruction, rupture and hemorrhage.

Gastrojejunocolic fistula.—As the name implies, this is a fistula between the stomach and colon by way of the jejunum. It is almost always the *result* of jejunal ulceration that follows a gastroenterostomy for a duodenal (90 per cent) or gastric (10 per cent) ulcer (Fig. 274). Rarely, it eventuates from a carcinoma of the colon or stomach. The jejunal ulcer appears from several weeks to several years with an average of about four years after the gastroenterostomy, and the fistula up to twenty-one years with an average of four to nine years after the operation. The causes of the jejunal ulcer are probably the same as those of the original gastric or duodenal ulcer (see gastric ulcer above). Some additional factors that have been incriminated are: operative trauma to the mucosa by way of the clamps, faulty technique, non-absorbable sutures, hematomas, and indiscretions in diet too soon after operation. The incidence of the fistula is difficult to determine, but the frequency of jejunal ulceration following gastroenterostomy is given as varying from 1.6 to 5 per cent. The lesion is practically confined to males, and the age limits are twenty to seventy years. *Symptoms* and *signs* are: (1) diarrhea (due to the short circuit or irritation of the small bowel) consisting of six to ten watery, semisolid or fatty stools a day, (2) eructation of gas with a fecal odor, (3) vomiting—this occurs

occasionally, but rarely contains fecal material, (4) pain of variable frequency, type and location, (5) emaciation, dehydration and weakness and (6) tenderness and rigidity in the left lower quadrant. The fistula is usually single, its edges on the jejunal side are smooth, while those on the colic side are indurated, the orifice is sharply defined, of varying sizes and when small it may be hidden by mucosal folds, and there is usually a peritoneal reaction with adhesions. The diagnosis is made from a history of ulcer treated by gastroenterostomy which is followed by return of ulcer symptoms, diarrhea, foul belching and wasting. It is confirmed roentgenologically by observing barium pass directly from the stomach to the



FIG. 274.—Gastroduodenocolic fistula. One end of the applicator is in the stomach (S) while the other end is in the colon (C). The jejunum (J) has been opened.

colon or vice versa. *Treatment* is surgical and consists of undoing the fistula, or block resection of the stomach, jejunum and colon. The *prognosis* is not good for the ulcers recur in from 40 to 60 per cent of the cases, fistulas recur in 12 per cent of the cases and the death rate is listed as varying from 15 to 27 per cent.

Intussusception—Invaginations of the stomach consist of stomach into esophagus, stomach into stomach and stomach into duodenum. The condition is not common. It has been described at all ages and has no predilection for either sex. It is almost always caused by a mucosal tumor that acts as a foreign body causing the contractions of the wall to propel it along the lumen. The intussusception may be (1) partial when only the mucosa is involved or complete when the entire wall is invaginated and (2) central when

the whole circumference is pulled in or lateral when only one of the surfaces is involved. In the gastroduodenal type, the invaginating segment may descend to the first, second or third portions of the duodenum. Initial *symptoms* are those produced by the tumor, but when intussusception occurs they are those of obstruction and consist of pain, vomiting and flatulence. After ingestion of barium, roentgenograms, in cases of incomplete obstruction, show a central area of translucency. In some cases, the pedicle of the tumor becomes gangrenous and the entire mass sloughs into the lumen. In most, however, *treatment* is disengagement of the segments and resection of the tumor and portion of the stomach.

Volvulus.—Volvulus of the stomach is an abnormal rotation which is reducible. The underlying *cause* is relaxed intra-abdominal ligaments and the contributing causes are obesity, trauma, marked weight loss and anomalous developments. The stomach may *rotate* partially or completely, anteriorly or posteriorly and along either the transverse or the longitudinal axis of the body. The condition is rare. The usual *history* consists of recurrent attacks of nausea and vomiting with epigastric pain. Occasionally there may be hematemesis and loss of weight. The *diagnosis* is made from a fluoroscope examination of the stomach after the ingestion of barium.

Foreign Bodies.—These are much less common in the stomach than they are in the air passages or the respiratory tract. They may be divided into those that form in the stomach—bezoars, and those that are swallowed. The word *bezoar* comes from the Arabic, Hebrew or Persian language and means that which counteracts poison. Its identification with concretions of the stomach is traced to the practice of utilizing such formations in the stomach and intestines of goats as the source of a tincture that was used against pestilence and poisons. Bezoars are of two types: (1) *Trychobezoars*—hair balls composed usually of hair and foreign material which, of course, are swallowed. They are, as a rule, built up in layers and may weigh as much as 5 pounds. They are frequently found in mentally deficient or insane, and are more common in women and children than in men. (2) *Phytobezoars*—vegetable concretions resulting from precipitation of the swallowed material in the stomach. At one time or another the following substances have been identified as contributing to the stones: persimmons, barks of trees, shellac, pumpkin residue, salol, grass, plant roots, bismuth, string, cocoanut fibers and tobacco. Bezoars may remain symptomless or they may cause diarrhea, anorexia, weakness, loss of weight, anemia, vomiting and flatulence. Roentgenograms after ingestion of barium show a mass covered by a thin film of radio-opaque material. *Treatment* consists of removal by way of a gastrotomy. *Foreign bodies* are *swallowed* by children, the mentally deficient, the insane, professional jugglers, those with perversion of appetite and for suicidal purposes. The objects swallowed are varied and consist of pins, needles, knives, razor blades, coins, bones and so forth. If the objects are small, and if the numbers are few, they will often pass through the stomach and intestines and be expelled in the feces. If the numbers are

large, then they tend to interlock and lodge. In the stomach they gather in the dependent portion and cause the organ to sag. *Symptoms* are the same as they are in the case of bezoars. Some of the objects can be removed from the stomach esophago-scopically, but others only by way of gastrotomy.

Obstruction—Obstruction of the stomach can be caused by many of the conditions already considered in this chapter, namely, (1) *congenital*—stenosis or stricture of the pylorus, (2) *inflammatory*—chronic hypertrophic gastritis, ulcer, actinomycosis, syphilis and tuberculosis, (3) *tumors* both benign and malignant and (4) *mechanical* disturbances—intussusception, volvulus and foreign bodies. In addition, there is an *acute dilatation* of the stomach caused by compression of the duodenum by the superior mesenteric artery. Predisposing causes for this type of obstruction are emaciation, ptosis, short mesentery and lordosis. The lesion occurs after trauma, post-operatively or during the course of unrelated diseases. *Signs and symptoms* consist of vomiting, pain, hiccough, distension of the abdomen, weight loss, emaciation and thirst. Roentgenograms show a dilatation of the duodenum. *Treatment* consists of keeping the stomach empty and replenishing the lost electrolytes. The *prognosis* is good.

Rupture—Rupture of the stomach when unassociated with a penetrating abdominal wound is spoken of as subperitoneal or subparietal rupture. It is not common. It affects males twice as frequently as females and has been described at all ages. It may be caused by (1) a direct blow, a kick or crushing injury, (2) by indirect force such as falling on the head or (3) by sudden and severe contraction of the abdominal wall, as by vomiting, particularly when the stomach is distended with food or gas. A predisposing factor in cases of overdistension is weakening of the gastric wall due to paralysis of the nerves and to interference with circulation. The lesion consists of (1) a partial tear of the mucosa, muscle or serosa. Tears of the mucosa may be associated with hematemesis while others produce no specific symptoms, and (2) a complete tear which results in shock, hemorrhage and later peritonitis. The *diagnosis* of a complete tear is confirmed by demonstrating a pneumoperitoneum roentgenographically. *Treatment* in partial tears is symptomatic, whereas in complete tears it is immediate laparotomy. The *mortality* rate in cases recorded in the literature is about 70 per cent.

Hemorrhage into the stomach may be massive when caused by an erosion of a vessel, or slight and prolonged when due to venous or capillary oozing. It may be evidenced by hematemesis, melena or occult blood in either the vomitus or stools. In 90 per cent of the cases, it is due to the following gastroduodenal lesions, ulcer, varices, gastritis, tuberculosis, syphilis, carcinoma, benign tumors, diaphragmatic hernia, trauma to abdomen, erosions from foreign bodies, and hereditary hemorrhagic telangiectasia. Other conditions which account for the remaining 10 per cent of hemorrhages are (1) blood dyscrasias such as leukemia, aplastic anemia, hemolytic icterus and purpura, (2) infectious diseases such as malaria, yellow fever,

cholera, scarlet fever and variola and (3) diseases of the heart and lungs associated with circulatory failure and increased venous pressure.

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cholera, scarlet fever and variola and (3) diseases of the heart and lungs associated with circulatory failure and increased venous pressure.

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Chapter XI

SMALL INTESTINE

EMBRYOLOGY

SINCE the *small and large intestines* are closely related embryologically, they will be considered together in this section. As in the esophagus and stomach, the original entodermal tube forms the epithelial lining and the investing splanchnic mesoderm gives rise to the connective tissue, muscle and peritoneum. At four weeks of embryonic life, the intestine is a *single tube* that is interrupted only in its mid-portion by the attachment of the vitelline duct (yolk stalk). Shortly thereafter, a ventral flexion becomes accentuated and a bulge in the caudal portion forms the cecum. An *anticlock-wise rotation* carries the cranial portion to the right and inferiorly and the caudal portion to the left. Following this, there is a rapid disproportionate elongation of particularly the small intestine, so that at seven weeks most of the tract herniates into the umbilical cord. Three weeks later, the small intestine *re-enters* and its caudal portion fills the left side of the abdomen compressing the lower part of the colon to the left. The large intestine re-enters last, and the cecal portion is carried to the right where it is fixed to the posterior wall. The *vermiform appendix* arises from the distal end of the cecal sac. The terminal portion of the *rectum* comes from the cloaca and the anal canal arises from a short ectodermal proctodeum. At six and seven weeks, a proliferation of the lining epithelium produces throughout the intestines scattered temporary occlusions of the lumen which are later recanalized by vacuolization.

ANATOMY

The small intestine measures 6.5 meters in length, extends from the pylorus to the colon and consists of a curved short portion, the duodenum and a long coiled portion, the proximal two-fifths of which are called the jejunum and the distal three-fifths the ileum. The *duodenum* measures 25 cm. in length. It has no mesentery, is covered in part with peritoneum and encloses the head of the pancreas. The first part is directed up and to the right beneath the liver and gall bladder, and anterior to the gastro-duodenal artery, bile duct and portal vein. The descending portion covers the medial portion of the right kidney, lies behind the transverse colon and receives the bile and pancreatic ducts at the ampulla of Vater. An angulation at the level of the fourth lumbar vertebra carries the third portion across the inferior vena cava and another angulation carries the distal part anterior to or to the left of the aorta. The coiled portion constitutes most of the small intestine. It is almost completely invested by peritoneum and is attached to the posterior abdominal wall by the mesentery. The demarcation between the

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between the columnar cells are goblet cells—easily recognizable because they are distended with mucus. At the bases of the villi are the crypts of Lieberkühn. Their depths contain (1) Paneth cells—These are large cells that disperse in their supranuclear portion numerous coarse eosinophilic granules, (2) scattered argentaffin cells which have round nuclei and fine subnuclear eosinophilic granules. These cells take a positive stain for silver and (3) in the region of the duodenal sphincter, the openings of Brunner's glands. These are branched, coiled mucous glands that for the most part are located in the submucosa. The lamina propria is composed of connective tissue containing argyrophilic fibers, and is heavily infiltrated with plasma cells, lymphocytes and eosinophiles. Aggregations of lymphocytes in the same layer form solitary lymph follicles and collections of these make up the Peyer's patches. The latter are found, as a rule, only in the ileum where they measure as much as 2 cm. across. The submucosa is composed of connective tissue and the muscularis of two spiral layers of muscle.

PATHOLOGY

Congenital Anomalies—Developmental malformations of the small intestine are relatively common. They may be listed as follows: umbilical hernia (omphalocele), failure of normal rotation, transposition, pancreatic inclusions, stenosis, atresia, diaphragms, duplications, cysts, diverticula, me-enteric cysts and Meckel's diverticulum.

Umbilical hernia or omphalocele is a protrusion of abdominal contents into an abnormal sac-like umbilical cord. Its origin may reflect a persistence of the normal fetal state at seven weeks of embryonic life, or it may represent a protrusion through an abnormal opening after the intestines have re-entered the abdomen. The sac consists of a translucent membrane (the stretched cord) which may easily rupture and result in evisceration. Most hernias are small and are amenable to surgical treatment.

Failure of normal rotation is usually limited to the last stage of the rotation in which case the mesentery fails to anchor along its base. This results in a freely movable ileum and cecum, and carries with it the danger of volvulus.

Transposition of the small intestine represents a mirror image of the normal, wherein the curve of the duodenum is on the left side, the root of the mesentery is directed from right to left and the ileum empties into the cecum in the left lower quadrant. It is accompanied by transposition of other abdominal viscera.

Pancreatic inclusions are found in all portions of the small intestine, but they are relatively more common in the duodenum and in Meckel's diverticulum. Currently, three popular theories are put forth to explain their presence: (1) portions of pancreas are transplanted from the original site during embryonic life, (2) they arise from metaplasia of the intestinal epithelium either during embryonic or postnatal life and (3) they represent a reversion to a more primitive phylogenetic type as seen in lower animals and

jejunum and ileum is arbitrary. The *jejunum* has a diameter of about 4 cm. and its walls are thicker, more vascular and redder. The diameter of the *ileum* is about 3.5 cm. The *mesentery* is fan shaped. Its root, measuring about 15 cm. in length, is directed obliquely from the left of the second lumbar vertebra to the right sacro-iliac joint. It crosses the horizontal portion of the duodenum, the aorta, inferior vena cava, right ureter and right psoas major muscle. The duodenum receives its *arteries* from the right gastric and superior pancreaticoduodenal branches of the hepatic and from the inferior pancreaticoduodenal branch of the superior mesenteric arteries, whereas the jejunum and ileum are supplied by the superior

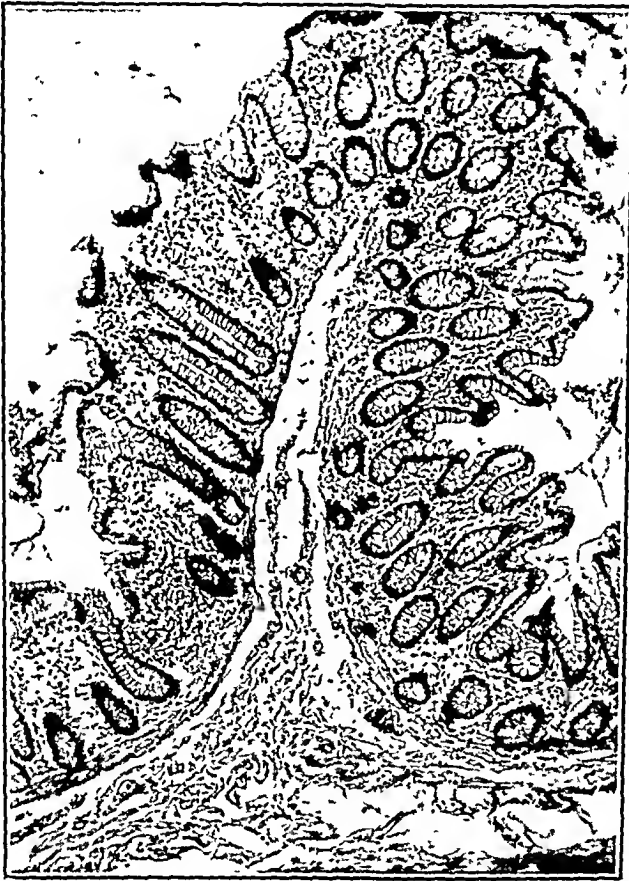


FIG. 275 —Section of small intestine showing a normal villus. x 37.5

mesenteric artery. The *veins* follow more or less the arteries. The *nerves* are derived from the vagus and splanchnic nerves through the celiac ganglia and the plexus around the superior mesenteric artery. The *lymphatic* vessels start in the mucosa as lacteals and end in the preaortic group of lymph nodes.

The *mucosa* of the small intestine contains *circular folds* (valvulae connentes) and villi, the purpose of which is to increase the surface area. The former are most prominent in the terminal duodenum and proximal jejunum where they measure as much as 8 mm. in depth. The *villi* cover all parts of the mucosa and measure as much as 1.5 mm. in length (Fig 275). They are lined with columnar *epithelium* that possesses a striated free border. Scattered

tended enough with fluid to produce pain and (3) the blood supply of the intestine is interfered with resulting in sloughing of the mucosa and hemorrhage. Physical examination may disclose a palpable movable non-tender intra-abdominal mass, visible peristalsis and abdominal distention. Obstruction, if present, is confirmed roentgenographically. Treatment is surgical extirpation of the mass, but because the lesion is usually intimately connected with the intestine proper, the latter must often be segmentally resected. If the disorder is recognized and treated early the prognosis is fair.

Diverticula of the small intestine may be congenital or acquired. Congenital diverticula are formed in the same way as are duplications and cysts, namely, by megacolon emulations of the solid stage of the intestine during embryonic development. They are true out-pocketings and contain all the layers of the intestinal wall. Acquired diverticula consist either of all the coats of the gut or of all



FIG. 276.—Several diverticula in the concavity of the jejunum.

but the muscle layers. They occur at weak spots in the wall, namely, at the entrance of the bile and pancreatic ducts and blood vessels, or in areas where the muscle has degenerated. The incidence of diverticula of the small intestine is given as from 0.16 to 5.85 per cent. They have no predilection for either sex, are rarely discovered before the age of thirty years and are usually seen in the sixth decade. They are single or multiple, ordinarily measure 3 to 4 cm. in greatest diameter, and communicate with the lumen of the intestine by narrow or wide ostia. In the duodenum, two-thirds of the lesions are found along the concavity of the second portion near the entrance of the ampulla of Vater. In the rest of the small gut, most of them are located along the mesenteric border of the upper and middle third of the jejunum (Fig. 276). Uncomplicated diverticula are, as a rule, symptomless although those in the duodenum are reputed to produce upper abdominal discomfort or pain, nausea and vomiting. When infected duodenal diverticula may simulate

fishes, where pancreatic tissue is dispersed through the intestines, liver and peritoneum.

Stenosis, atresia and diaphragms occur in any portion of the small intestine, but they prevail in the duodenum. A *stenosis* connotes a narrowing of the lumen, *atresia* a complete closure (both over segments of varying lengths) and a *diaphragm* a membranous band that partially or completely traverses the lumen. Although many theories have been advanced from time to time to explain these anomalous formations, it is probable that the abnormalities are caused by a failure of the lumen to recanalize properly following the obliterative phase of development. In the *duodenum*, one-third of the lesions are found in the vicinity of the opening of the common bile duct, another third at the duodenojejunal junction and the rest in other portions. There is no predilection for sex or race. Clinically, if the obstruction is partial it may cause little disturbances, but if it is severe or complete it is accompanied by vomiting soon after birth. If the occlusion is proximal to the ampulla of Vater, the vomitus will be free of bile and material passed by rectum will be bile stained, but if it is below this level the opposite is true. After the initial episodes, blood in the vomitus is a constant finding. Examination discloses a distended epigastrium, a soft mass in the region of the duodenum, visible gastric peristalsis, and, roentgenographically, gas and fluid levels in the stomach and duodenum. If the obstruction is in the *jejunum* or *ileum*, the only clinical differences are that the entire abdomen is distended and the gas and fluid levels occupy varied portions of the small intestine. The only effective *treatment* is early surgical restoration of the lumen of the bowel. It should be stressed that at operation all portions of the intestine must be examined for the occlusions are sometimes multiple. The *mortality* rate is high.

Duplications and cysts of the small intestine can be considered together for their genesis and clinical findings are similar. They have also been *called* reduplications, enteric cysts, enterogenous cysts, ileum duplex and giant diverticula. They too arise from abnormal recanalizations of the solid stage of embryonic development. The only difference between a duplication and a cyst is that the former connects with the intestinal lumen while the latter does not. Each contains most of the layers of the bowel wall. It is apparent that theoretically these abnormalities may be of many shapes and sizes and that they may have variable connections with the bowel. Thus a duplication may be several to many centimeters long and be connected with the main lumen at either end or anywhere along its course. The cysts are round, oval or elongated and are distended with fluid. The duplications or the cysts may be intramural or extramural. The latter are frequently between the folds of the mesentery, but they may be along the free border of the gut and have their own mesentery. As a rule, however, some portion is intimately attached to the main alimentary tract. Most of the duplications and cysts occur in the *ileum*. As a rule, they are found in children and are *symptomless until* (1) they obstruct the lumen of the gut from pressure of the mass, (2) they become dis-

tended enough with fluid to produce pain and (3) the blood supply of the intestine is interfered with resulting in sloughing of the mucosa and hemorrhage. Physical examination may disclose a palpable movable non-tender intra-abdominal mass, visible peristalsis and abdominal distention. Obstruction, if present, is confirmed roentgenographically. Treatment is surgical extirpation of the mass, but because the lesion is usually intimately connected with the intestine proper, the latter must often be segmentally resected. If the disorder is recognized and treated early the prognosis is fair.

Diverticula of the small intestine may be congenital or acquired. Congenital diverticula are formed in the same way as the duplications and cysts, namely, by irregular emulations of the solid stage of the intestine during embryonic development. They are true out-pocketings and contain all the layers of the intestinal wall. Acquired diverticula consist either of all the coats of the gut or of all



FIG. 276.—Several diverticula in the concavity of the jejunum.

but the muscle layers. They occur at weak spots in the wall, namely, at the entrance of the bile and pancreatic ducts and blood vessels, or in areas where the muscle has degenerated. The incidence of diverticula of the small intestine is given as from 0.16 to 5.55 per cent. They have no predilection for either sex, are rarely discovered before the age of thirty years and are usually seen in the sixth decade. They are single or multiple, ordinarily measure 3 to 4 cm. in greatest diameter, and communicate with the lumen of the intestine by narrow or wide ostia. In the duodenum, two-thirds of the lesions are found along the concavity of the second portion near the entrance of the ampulla of Vater. In the rest of the small gut, most of them are located along the mesenteric border of the upper and middle third of the jejunum (Fig. 276). Uncomplicated diverticula are, as a rule, *symptomless* although those in the duodenum are reputed to produce upper abdominal discomfort or pain, nausea and vomiting. When infected duodenal diverticula may simulate

acute cholecystitis, duodenal ulcer or pancreatitis and jejunal diverticula are indistinguishable from appendicitis. Other *complications* common to both duodenal and jejunal diverticula are: inflammatory perforation, local abscess, peritonitis, adhesions, intestinal obstruction, ulceration, hemorrhage, and secondary malignant tumor formation. In addition, those in the duodenum may be accompanied by obstruction to the common bile duct and those in the jejunum by formation of concretions with dislodgement and intestinal obstruction, by traumatic rupture and volvulus. *Treatment* will depend entirely upon the type of accompanying complication. In asymptomatic cases, no therapy is necessary.

Mesenteric cysts.—The term mesenteric cyst merely connotes a cyst within the mesentery, and as such includes not one type but



FIG. 277 —Mesenteric cysts of intestinal (left) and lymphatic (right) origin.

many types of cysts. They may be *divided into* (1) those arising from embryonic remnants, such as sequestrations of the intestine or pinched off intestinal diverticula, lymphatic channels, germinal epithelium of the ovary, Wolffian body or Mullerian ducts, (2) those of inflammatory origin, such as echinococcus disease or degeneration of a tubercular mass and (3) those arising as a degeneration of a malignant tumor, such as a myosarcoma or fibrosarcoma. The incidence is given as 1 in 100,000 hospital admissions; females are affected somewhat more frequently than males, and they are found at all ages from fetuses to the aged. Early, there are no *symptoms* and the tumor may be discovered by palpation alone or by distention of the abdomen. Later, symptoms are those of the *complications* which consist of the following: (1) Intestinal obstruction. This occurs ultimately in about one-half of the cases and is due to em-

bracing of the bowel by the mass, to simple compression or to torsion of the cyst. The obstruction may be partial and chronic or acute, or it may be complete. (2) Peritonitis consequent to intestinal obstruction or rupture of the cyst. (3) Hemorrhage into the cyst from erosion of a vessel and (4) Rupture of the cyst. Roentgenograms will occasionally disclose a shadow.

Pathologically, as would be expected, the cysts are of various types. The two most commonly encountered, however, are those originating in intestinal sequestrations or diverticula and those consisting of dilated lymphatic channels. Sometimes both types are found in a single specimen (Fig. 277). The size varies from a

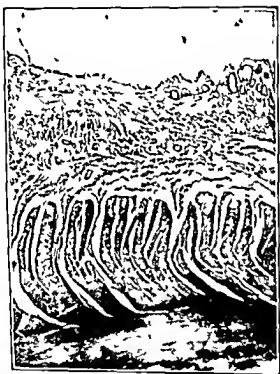


FIG. 278 — Mesenteric cyst showing intestinal muscles, fibrosis of the submucosa and a gradual disappearance of the mucosa. $\times 375$

few millimeters to 30 cm. or more in diameter. Cysts of *enteric* origin are usually unilocular and have walls that measure as much as 1 cm. in diameter. The inner surface is smooth or rough, and the lumen contains colorless or brown mucoid material. *Histologically*, the wall of the smaller cysts may duplicate that of the intestine (Fig. 278). As the cyst becomes larger, however, the mucosa first disappears and is replaced with fibrous tissue and later the muscle layers are also absorbed. In the end, the structure consists of a mass of hyalinized fibrous tissue in which there are scattered lymphocytes and lymph follicles. *Lymphogenous* cysts are often multilocular, have thin transparent walls, and are filled with clear straw colored or hemorrhagic fluid. *Histologically*, their

walls are formed of thin strands of connective tissue lined by a single layer of endothelial cells.

A precise preoperative *diagnosis* is difficult for there are many cysts and tumors in the abdomen that will clinically duplicate mesenteric cysts. *Treatment* is enucleation of the tumor accompanied by resection of the intestine when necessary. Marsupialization is performed when the patient cannot tolerate a more extensive procedure. The *prognosis* is good in the absence of complications, but is attended by a 35 to 50 per cent *mortality* when resection of the bowel is necessary.

Meckel's diverticulum is only one of a group of anomalies that arise from the *vitelline duct*. The *others*, although rare, may be listed as follows: (1) Persistence of the entire duct forming a *fistula* between the intestine and the umbilicus. Escape of intestinal contents in such cases causes excoriation of the skin of the abdomen.



FIG. 279.—Meckel's diverticulum.

(2) *Complete obliteration* of the duct leaving a persistent fibrous cord that connects the umbilicus with the ilium. (3) *Obliteration* of only a *segment* of lumen anywhere along the original course. (4) *Dilation* of the patency to form a central or terminal *cyst*.

A Meckel's diverticulum is a *diverticulum* that forms from the intestinal portion of the vitelline duct. It is a blind pouch usually with a wide ostium that measures 1 to 3 cm. in length and is located in the ante-mesenteric border of the ileum (Fig. 279). In infants, it is found 30 to 46 cm. and in adults about 107 cm. proximal to the ileo-cecal valve. Its incidence is reported as 1 to 4 per cent of the general population. It is usually discovered between the ages of ten to thirty years, and is three times as frequent in males as it is

in females. The anomaly is *symptomless* until complications arise. These may be grouped as follows: (1) *Inflammation* which may be acute and severe or chronic and mild. Symptoms in such instances are indistinguishable from those of appendicitis. (2) *Peptic ulceration* of the adjacent intestinal mucosa. This is due to secretion of hydrochloric acid and pepsin from heterotopic gastric mucosa. Such aberrant tissue is found in 25 per cent of all diverticula and probably arises as a proliferation of pluripotent primitive entodermal cells that have been incorporated in the diverticulum. Symptoms of ileal ulcer are the same as those of duodenal ulcer. They may erode a vessel and produce intestinal hemorrhage or they may perforate the bowel and cause peritonitis. Other heterotopic tissues encountered are pancreatic, biliary, duodenal and colonic. (3) *Obstruction*. This may be mild or severe and partial or complete. It is due to volvulus of the ileum about a persistent cord or to intussusception. The latter arises as a result of the diverticulum itself or as a result of tumor formation at its base. (4) The development of both benign and malignant tumors. Some of those described are carcinoid, enterocystoma, adenoma, carcinoma and sarcoma. The diagnosis of Merkel's diverticulum with its various complications is difficult. It is most often confused with acute appendicitis. Treatment consists of surgical removal. In diverticula that are the seat of pathologic changes, the mortality rate is recorded as varying from 9.3 to 47 per cent.

Inflammation—Non-specific Inflammations—These consist of acute phlegmonous enteritis and duodenal ulcer.

Acute phlegmonous enteritis is analogous to phlegmonous gastritis which has been described in the preceding chapter. It is an uncommon condition that is caused by pyogenic organisms among which the *streptococci* predominate. The route of infection is by way of the blood stream or directly through the mucosa. *Predisposing factors* for the latter are abdominal trauma, foreign bodies, intestinal parasites and portal stasis and for the former pneumonia, scarlet fever and tonsillitis. The disease is present at all ages but predominates between thirty and seventy years, and it affects males three times as often as females. *Symptoms and signs* consist of sudden epigastric or peri-umbilical pain, constant sometimes fecal vomiting, constipation, less commonly diarrhea, rarely melena, fever, leukocytosis, abdominal distention and tenderness, and jaundice if the lesion is in the duodenum.

The jejunum is involved most frequently, followed by the duodenum and then the ileum. The *involved segment* measures from 4 to 60 cm. in length and is sharply or indistinctly demarcated from the adjacent normal bowel. The serosa is red, edematous and covered with fibrinous or yellowish grey foci, the wall is thick, heavy and rigid, the submucosa is edematous and measures 1 cm. or more in thickness, the mucosa is grey and intact or superficially ulcerated, the circular folds are swollen and rigid, the lumen is greatly reduced in size, the mesentery is thick and indurated, and if the lesion is in the duodenum, the pancreas becomes secondarily involved. In almost all cases, there is a localized fibrous peri-

tonitis while in a few, even without perforation, peritonitis is generalized. *Histologically*, as in the stomach the characteristic changes are severe edema and diffuse infiltration with neutrophils.

A pre-operative *diagnosis* is virtually impossible. *Treatment* is segmental resection of the bowel. The *mortality* rate is high.

Duodenal Ulcer.—The theories regarding the *causes* of duodenal ulcer are the same as those described in the preceding chapter on gastric ulcer. A word or two, however, should be added concerning an acute ulcer that follows cutaneous burns (*Curling's ulcer*). The *causes* of this lesion have also been the subject of much speculation. The most reasonable explanation appears to be as follows. Cutaneous burns are usually accompanied by mild or profound shock, and shock is manifested by a generalized capillo-venous atony and congestion. In the duodenum, as in the rest of the gastro-intestinal mucosa, this congestion is followed by erythrocytic diapedesis and extravasation amounting in some cases to ecchymoses. It has been demonstrated that such a mucosa is vulnerable to otherwise inconsequential trauma (such as might occur from food or gastric juice) and, in fact, that it is often the seat of superficial erosions. An extension of the latter results in acute ulceration.

Clinically, duodenal ulcer appears to be more frequent than gastric ulcer, although actually the incidence is about the same. The sex, age distribution, symptoms and signs are similar to those outlined in the section on gastric ulcer except, of course, that the crater is demonstrated radiologically in the first portion of the duodenum. *Pathologically*, the lesion is almost always found within 2.5 cm. of the pylorus (Fig. 280) and presents the same gross and microscopic features as does gastric ulcer. If healing does not take place, the ulcer may result in the following: (1) *Hemorrhage*. This occurs in about 13 per cent of all cases and when severe is usually the result of erosion of the pancreaticoduodenal artery. (2) *Perforation*. If the ulcer is located on the posterior wall it will penetrate into the pancreas where it may produce an abscess or pancreatitis. If it is located on the anterior wall, it will perforate into the peritoneal cavity in the absence of adhesions or into the gall bladder, liver or other organs if there are preformed adhesions. Perforation into the peritoneal cavity is accompanied by the symptoms and signs already enumerated in the section on gastric ulcer (p. 344). (3) *Obstruction*. This may be due to fibrotic stenosis of the duodenum or simply to edema and spasm consequent to the irritation produced by the ulcer. The symptoms are those of any duodenal obstruction. It is to be noted that carcinoma practically never occurs as a complication of duodenal ulcer.

The *diagnosis* of duodenal ulcer is made from a history of epigastric pain that has a definite relation to food, and by demonstrating the crater roentgenographically. *Treatment* is medical and surgical. As in gastric ulcer *medical* therapy consists of a bland diet, antispasmodics, sedatives, antacids and psychotherapy. *Surgical* therapy is definitely indicated in severe hemorrhage, perforation, obstruction and the presence of intractable pain. The old operation of simple gastroenterostomy has in recent years been superceded by

resection of the ulcer itself and of the acid bearing portion of the stomach. Even more recently, *resection of the vagus nerves* either supradiaphragmatically or infradiaphragmatically has been reported as having a salutary effect. The *indications* for its employment have been listed as (1) cases previously operated upon where a new ulcer has formed, (2) the presence of intractable pain or pain associated with environmental stress that responds to antacids, (3) repeated hemorrhage and (4) perforation. It is said to be *contraindicated* (1) when the patient is psychotic or psychoneurotic and the pain is not relieved by antacids, *i.e.*, it is not due to the ulcer, (2) in patients that are bleeding and (3) when there is fibrotic stenosis.



FIG. 280 — Acute duodenal ulcer

The physiological changes reported as developing consequent to sectioning of the vagus nerves have been enumerated under the causes of gastric ulcer. Here it is sufficient to state that on the basis of preliminary reports, there appears to be an immediate and sustained alleviation of the ulcer symptoms and a healing of the defect. Disturbing side effects sometimes encountered consist of diarrhea, fullness and sensations of pressure in the epigastrium, weakness, and, most troublesome of all, *chronic gastric dilatation*. Whether the gastric dilatation and retention will outweigh the initial benefits or whether other as yet unrecorded ill-effects will develop in vagotomized patients, time alone will tell for the operation is too recent to be properly evaluated. The *prognosis* in duodenal ulcer parallels that in gastric ulcer.

Specific Inflammations.—Granulomatous lesions of the small intestine may be grouped into four categories, (1) Boeck's sarcoid, (2) syphilis, (3) tuberculosis and (4) regional enteritis

Boeck's sarcoid is so uncommon that little space need be devoted to it here. The intestines have been reported to be involved in a few cases of the disseminated form of the disease and in a still fewer number of cases has the disease been recorded as primary and localized to the small bowel. *Clinically*, the disorder simulates regional enteritis. There are lassitude, loss of weight, nausea and vomiting, anorexia, and diarrhea. By roentgen examination, however, it is said to lack the "string sign" of regional enteritis; the mucosal pattern is that of swelling and hypertrophy of the folds rather than denudation, and the changes are more diffuse than segmental. *Grossly*, short or long portions of the bowel are externally rough, granular and shaggy; the wall is thick and fibrotic; the mucosa is diffusely and uniformly covered with nodules measuring 2 to 4 mm. in diameter and it may be superficially ulcerated, and the lumen is reduced in caliber. *Histologically*, the characteristic unit is the solid epithelioid tubercle.

Syphilis of the intestines constitutes less than 2 per cent of all syphilitic lesions. *Clinically*, it may be divided into (1) *congenital* syphilis which is characterized chiefly by diarrhea and cannot be differentiated from simple enteritis or tuberculosis, (2) *acquired secondary* syphilis which is characterized by malaise, diarrhea, cramplike pains and fever and (3) *acquired tertiary* syphilis in which there is at first diarrhea, blood and pus in the stools, colicky pains and tenesmus, and later progressive obstruction with constipation or constipation alternating with diarrhea. The *congenital* form of the disease is usually encountered in stillborn infants, those dying soon after birth or those dying in early childhood. *Grossly*, the lesions appear as raised, yellow, broad bands that occur at irregular intervals and tend to encircle the bowel. Some disclose multiple ulcerations. *Histologically*, there are either miliary gummas or there is a diffuse infiltration with plasma cells and lymphocytes. The inflammatory cells as in other syphilitic lesions are grouped around vessels and these show the usual endarteritis obliterans and peri-endophlebitis. In *acquired secondary* syphilis, the lesions are those of acute enteritis. In *acquired tertiary* disease, there are mucosal and submucosal raised infiltrations which break down, ulcerate, extend, encircle the bowel and upon healing produce stenosis. The ulcers have greyish white necrotic floors, hard bases and may perforate to produce a localized abscess or peritonitis. *Histologically*, they reveal either small gummas or the usually diffuse inflammatory infiltration. A clinical diagnosis of syphilis is only presumptive and of , extremely difficult to make. A pathologic diagnosis can be made only histologically. The demonstration of spirochetes particularly in tertiary lesions is difficult. *Treatment* consists of antisyphilitic therapy and, when complications such as perforation and stenosis arise, appropriate surgical therapy. The *prognosis* in acquired secondary type is good, but in the others it is guarded. *Tuberculosis* of the intestine is caused by either the human or the

bovine strain of tubercle bacillus and is almost always brought about by swallowing the organisms in sputum or in contaminated milk. A few organisms ingested sporadically probably cause no harm, while a continuous and copious supply affect that segment of the bowel where there is temporary stasis of food and where there is an abundant supply of lymphatics, namely, the lower ileum. Tubercle bacilli pass through an intact mucosa without any detectable injury. They lodge in the summits of the solitary lymph follicles and Peyer's patches where they soon produce grey translucent pinpoint tubercles. These are surrounded by serum and erythrocytes. As the lesion increases in size the center softens and liquefies resulting in a 1 to 10 mm purplish red mucosal nodule. Involvement of the overlying mucosa produces ulceration, perforation and sloughing of the epithelium. This leaves a small ulcer with overhanging edges and paves the way for an immediate and intense secondary inflammation. Simultaneously, bacteria are carried along the lymphatics to adjacent and subjacent tissues where they form new tubercles and the process repeats itself. Ultimately, there are numerous grossly detectable mucosal tubercles, nodules and ulcers that first occupy the solitary follicles and Peyer's patches, but later, extend beyond these in an irregular manner. The lesions penetrate to varying depths and on the serosal surface are usually represented by numerous pinpoint tubercles that are often distributed in a cord-like fashion along the course of the lymphatics. In some cases, caseation and ulceration predominate (*ulcerative type*), while in others the reparative process predominates (*hyperplastic type*). The reparative process first consists of non-specific granulation tissue which is composed of fibroblasts, epithelium and inflammatory cells, and later of contracting dense fibrous tissue. This results in thickening, stiffening and tumefaction of the wall to produce a mass or a constriction that is easily mistaken for a neoplasm (Fig 281). In cases where the original ulcer is small and the destruction of tissue minimal, however, the consequent fibrous tissue contracts and the mucosa regenerates leaving little or no tell-tale evidence of a previous infection. The mesenteric lymph nodes are involved by the tuberculous process in about 25 per cent of cases.

Intestinal tuberculosis is found in 85 per cent of cases of pulmonary tuberculosis with cavitation and in 50 per cent of cases of pulmonary tuberculosis without clinical evidence of cavitation. The disease has no predilection for either sex and it occurs at all ages. Signs and symptoms are extremely variable. In some cases of pulmonary tuberculosis, any digestive disturbances, abdominal discomfort or simply merely failure to improve should suggest tuberculosis of the bowel. In others, there may be abdominal pain, diarrhea, constipation, diarrhea alternating with constipation, elevated or swinging temperature, loss of weight and blood in the stools. Roentgenograms disclose local and general increase of motility, spastic filling defects or complete obstruction. The complications are (1) stenosis and obstruction, (2) perforation which occurs in 37 per cent of all cases, (3) non-specific peritonitis (as a result of perforation), (4) fecal abscess and (5) amyloidosis. Treatment consists of general

anti-tuberculosis measures and of surgery when the first four of the aforementioned complications arise. The *prognosis* depends upon the general condition of the patient and the stage of the pulmonary disease.

Regional enteritis has also been *called* regional ileitis, terminal ileitis, acute ulcerative ileitis, specific inflammatory granuloma, non-specific ileocolitis, chronic cicatricial enteritis, ulcerating stenosing enteritis and Crohn's disease. It is a chronic specific granulomatous disease of the intestine of unknown etiology. Among the numerous *causative factors* that have been suggested are (1) bacteria as *B. coli*, *B. dysenteriae*, tubercle bacillus, bacillus acidophilus and anaerobic streptococci, (2) bacterial toxins, (3) viruses, (4) parasites, (5) allergy, (6) foreign bodies, (7) abdominal trauma, (8) impairment of blood supply, such as consequent to intestinal

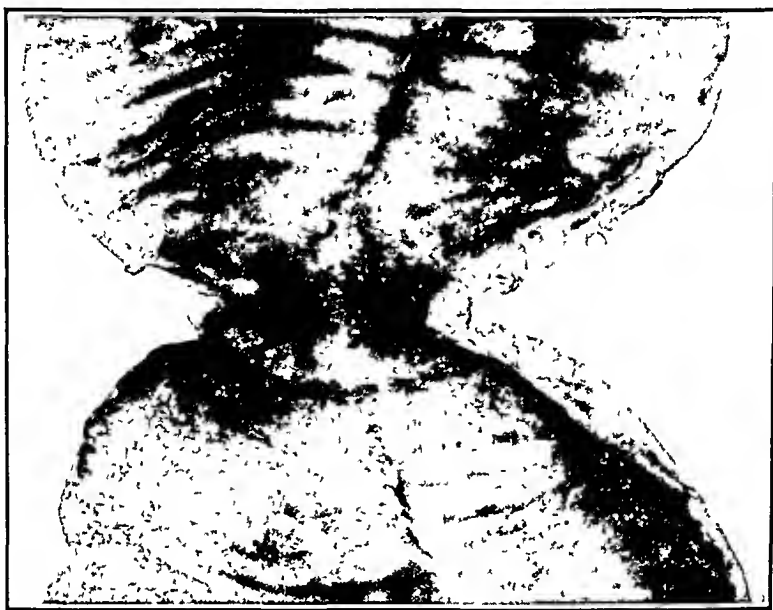


FIG. 281 —Tuberculous structure of the ileum The lesion is similar to constricting carcinoma shown in Fig 283 Another structure at the ileo-cecal valve was responsible for dilatation of the distal segment.

obstruction, partial volvulus, mesenteric thrombosis and incarcerated hernia and (9) low grade chronic lymphangitis with obstruction. The disease occurs at all ages with a peak incidence between ten and forty years, and affects three males to every two females. *Symptoms* are quite variable but ordinarily they may be grouped into four categories: (1) Those that are indistinguishable from acute appendicitis. There may be pain, tenderness in the right lower quadrant, fever and leukocytosis. (2) Those that mimic ulcerative colitis and present colicky abdominal pain, diarrhea, blood and mucus in the stools, malaise, loss of weight, secondary anemia and intermittent fever. (3) Those of chronic incomplete intestinal obstruction exhibiting abdominal cramps, borborygmus, visible peristalsis, intermittent vomiting and sometimes a visible mass. (4) Those consequent to fistulous formations with other organs, abdominal wall or fistula in ano. Roentgenograms with the aid of

barium disclose rigidity, a filling defect, a thin irregular linear shadow (string sign) or a complete obstruction.

The lesion may involve any portion of the small bowel and, occasionally, a segment of the large intestine, but it is most common in the lower portion of the ileum. It is usually single but may be multiple, and it involves several or many centimeters of the gut. In early cases, there is often some serous fluid in the peritoneal cavity. The involved segment shows a mottled red dull fibrin covered serosa, a thick edematous and indurated wall, and superficial ulcers of the mucosa, particularly opposite the mesentery. The mesentery is thick, edematous and contains enlarged lymph nodes. As the lesion progresses the serosa becomes fibrotic, thick and granular, the wall is broadened, rigid, unyielding, greyish white and fibrotic, the mucosa is irregularly ulcerated and the remaining islands of tissue becomes hyperplastic to form polypoid excrescences,

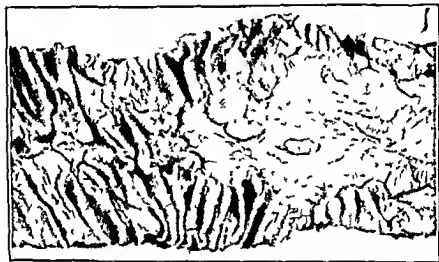


FIG 282.—Regional enteritis illustrating a sharp demarcation between healthy and diseased bowel, irregular ulcers and prominent residual islands of mucosa.

and the lumen is greatly reduced in caliber or completely occluded (Fig 282). As a rule, the involved segment is sharply demarcated from normal bowel, kinks may form as a result of adhesions, and the lumen proximal to the lesion may be dilated. *Histologically*, the acute lesions reveal a fibrino-purulent exudate covering the ulcers, an infiltration of the wall with neutrophils and edema and hemorrhage in the serosa. Later, the mucosa is partly or entirely eroded and replaced with non-specific inflammatory cells among which neutrophils are abundant, the submucosa and rest of the wall is greatly thickened first by granulation tissue and later by fibrous tissue, and there are often focal collections of mononuclear cells with peripheral giant cells forming spurious tubercles. The draining lymph nodes reveal congestion, dilated lymphatics, edema, an infiltration with plasma cells and fewer neutrophils, focal collections of mononuclear cells forming "tubercles" similar to those in the bowel and no fibrosis.

The *diagnosis* is made from a consideration of the history and from roentgenographic studies. Clinically, the lesion is confused with almost any pathologic condition in the abdomen but particularly, with acute appendicitis, ulcerative colitis and hyperplastic tuberculosis of the small intestine. *Treatment* is difficult. In acute stages the consensus appears to be to do nothing surgically, for it has been shown that some of the lesions regress spontaneously. In chronic stages, wide resection of the involved segment together with a wedge of mesentery relieves all symptoms (temporarily at least) in two-thirds of the cases. The *prognosis* must remain in doubt for many years because recurrences and complication, such as intestinal obstruction and fistulas, are common. Permanently good results are obtained in only 50 per cent of cases.

Tumors.—From a histogenetic point of view, neoplasms of the small intestine may be classified as follows: From the epithelium there may arise an adenoma, papilloma, carcinoma and carcinoid; from connective tissue, a fibroma, fibrosarcoma, myxoma and myxosarcoma; from fat, a lipoma and theoretically a liposarcoma; from vessels, a lymphangioma, hemangioma and hemangiosarcoma; from nerves a neurofibroma and neurofibrosarcoma; from muscle, a leiomyoma and leiomyosarcoma; from lymphoid tissue (reticulum cells), a plasmacytoma and lymphoblastoma which includes lymphosarcoma, Hodgkin's disease and reticulum cell sarcoma; from normal tissues abnormally arranged or from embryonically misplaced tissue, a myoepithelial hamartoma, and from foreign tissues, secondary neoplasms and endometriosis.

The *signs* and *symptoms* produced by tumors of the small bowel are quite similar regardless of whether the neoplasm is benign or malignant, or whether it involves the duodenum, jejunum or ileum. Treatment, basically, is also the same. In order, therefore, to save space and spare useless repetition they may be considered forthwith. The onset of symptoms may be insidious and over a period of many months or years or it may be abrupt. The former is due merely to the presence of the *tumor* or to *gradual* and partial *obstruction*. In such cases there may be any combination of the following: vague abdominal distress or pain (located in the epigastrium if the duodenum or upper portion of the jejunum is involved or in the lower abdomen or right lower quadrant if the lower portion or the terminal ileum is involved), anorexia, weakness, loss of weight, nausea, vomiting (which may contain blood, bile if the lesion is below the ampulla of Vater, and fecal material if it is in the distal portion of the bowel), melena or occult blood in the stools, secondary anemia, diarrhea, constipation, diarrhea alternating with constipation, and jaundice. Onset of sudden symptoms means *acute* and usually complete *obstruction*. This may be heralded by any of the aforementioned symptoms and signs of it may be the first indication that something is amiss. It is due to direct occlusion of the lumen by the *tumor*, to an *intussusception* or, rarely, to a *volvulus*. In such instances, there is a sudden sharp colicky agonizing pain in the epigastrium or the right lower quadrant which is associated with vomiting, shock, emptying of the bowel and blood and mucus in

the stools. Physical examination discloses a distended abdomen, visible peristalsis, borborygmi and a palpable mass. Roentgenograms, with or without the aid of barium, are extremely helpful in at least localizing the site of the lesion. They may disclose an obliteration of the normal rugie, a crater like defect, a decreased area of density due to a polypoid intraluminal mass, residuum of barium in the involved loop or complete obstruction. Treatment of benign tumors is local excision if this is feasible, or segmental resection of the bowel if it is not. Treatment of malignant lesions is wide segmental resection of the involved intestine together with all possible diseased tissue and lymph nodes. In the jejunum and ileum, this usually means a wedge of the mesentery, while in the duodenum, it might mean part or all of the head of the pancreas. Postoperative irradiation in cases with malignant neoplasms is optional in all but the lymphoblastomas where it is mandatory.

Further specific consideration will be devoted to the following benign tumors, adenoma, hemangioma and lipoma and to the following malignant tumors, carcinoma, sarcoma, neurofibrosarcoma, leiomyosarcoma, lymphoblastomas and secondary neoplasms.

Adenoma—The same distinction should be made among adenoma, papilloma and polyp in the small intestine as has been outlined for similar tumors in the stomach. Adenomas constitute from 30 to 40 per cent of all benign tumors and about 8 per cent of all types of growths of the small intestine. Most of them are asymptomatic and are discovered at autopsy. They have been found at all ages from six months to the seventh decade and have no predilection for any race or either sex. They are more common in the lower portion of the small bowel, are usually single but may be multiple, and always bulge into the lumen. Their size varies from a few millimeters to 2 or 3 cm in diameter. They may be sessile or pedunculated, and if the latter, the pedicles may be broad and squatty or long and slender. In either case, the free portion is usually expanded to form a mushroom-like mass that is smooth, granular or creviced. The adenoma is light grey to deep red, soft to moderately firm and freely movable at its mucosal attachment. Histologically, the core is composed of a well-vascularized connective tissue stalk, often infiltrated with neutrophils, lymphocytes, plasma cells and erythrocytes. At the base, the covering epithelium does not differ greatly from normal, while at the tip, it forms numerous glands that are somewhat irregular. The lining cells are 3 to 4 layers thick, have lost their polarity, and disclose granular deeply eosinophilic cytoplasm and hyperchromatic round or oval nuclei. Mitoses are often numerous. Two complications that adenomas are subject to are a transformation to carcinoma and intussusception.

Hemangioma—This is a comparatively rare tumor of the small intestine, but it is extremely important for it may result in fatal hemorrhage. Bleeding usually starts in infancy but is not necessarily detected until the patient develops severe anemia, asthenia and cachexia. Any portion of the bowel may be involved and the lesions are single or multiple. Grossly, they appear as deep red or purple

masses a few millimeters in diameter, as diffuse permeations of long segments of the intestine, or, most commonly, as polypoid masses projecting into the lumen. *Histologically*, they are of the cavernous, capillary or endotheliomatous type.

Lipoma.—Lipoma of the small bowel is relatively common, there having been about 275 cases recorded in the literature. Their chief importance lies in the fact that they are often the cause of an intussusception. Males are affected as frequently as females, and the most common age groups are from the third to the sixth decade. The ileum is involved more often than the duodenum or the jejunum. Nine-tenths of the lesions are located in the submucosa and the rest are found in the serosa. (In the large intestine, the reverse is true.) The *tumors* are usually single but may be multiple. They are sharply circumscribed and encapsulated, round or oval, polypoid



FIG. 283.—Constricting carcinoma of the ileum with dilatation of the bowel proxima to the growth. Compare with tuberculous stricture in Fig. 281.

or sessile, moderately firm and measure as much as 15 cm. in diameter. Cut surfaces present the usually light yellow fatty tissue separated into lobules by connective tissue septa that originate in the capsule. *Histologically*, lipomas are composed of adult fat cells. The *prognosis* is good unless there is accompanying obstruction or intussusception, when the mortality reaches as high as 50 per cent of all cases operated upon.

Carcinoma.—Carcinoma of the small intestine constitutes about 60 per cent of all malignant tumors of this portion of the bowel and from 0.3 to 4.9 per cent of all cancers of the gastrointestinal tract. The *cause* of the relative *immunity* from malignant neoplasms is not known, but it has been said to be due to the fluid contents of the intestine, to the alkalinity of the chyme and to the absence of sharp curves. It is most prevalent in the sixth decade and attacks men twice as frequently as women. The distribution of the lesions in

the small bowel is approximately equal among the *duodenum*, *jejunum* and *ileum*. In the *duodenum*, about one-half of the growths are located around the ampulla, one-third proximal to the ampulla and the rest distal to the ampulla. Grossly, carcinomas of the small intestine are of three types, namely, infiltrative, ulcerative and polypoid. *Infiltrative* lesions are the most common. The mucosa is usually intact for a long while, and only late does it tend to ulcerate. The growth rapidly penetrates into the submucosa and between the muscle bundles to produce an ill-defined greyish white, firm thickening of the entire wall. The tumor, as a rule, measures 2 or 3 cm. or less in length, and by contracting produces partial or complete occlusion of the lumen (Fig. 283). The second most common type of growth is the *ulcerating* variety. It too tends to

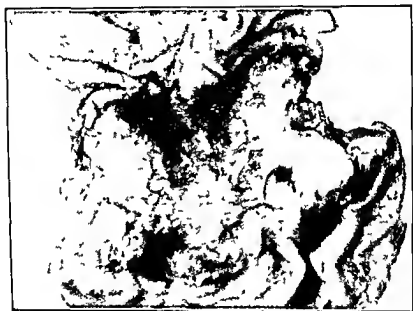


Fig. 284—Ulcerating carcinoma of the duodenum

infiltrate the bowel wall, but as it does so it simultaneously ulcerates (Fig. 284). The excavation frequently keeps pace with the neoplasia, thereby producing a large crater surrounded by elevated edges of firm grey tumor tissue. The lumen in these cases is often dilated instead of constricted. This type of growth may result in perforation of the bowel or in erosion of a vessel with massive or fatal hemorrhage. The least common type of carcinoma is the *polypoid* variety (Fig. 285). It grows primarily into the lumen and produces symptoms by obstruction or intussusception. The mass as a rule measures less than 5 cm. in diameter. Its mucosal surface is smooth or fissured and intact or superficially ulcerated. The base is usually sessile and its attachment to the wall is secure. The tumor is moderately firm and pinkish grey or light brown. *Histologically*, carcinoma of the small bowel is similar to that of the stomach. The adenomatous and anaplastic varieties, however,

predominate whereas the signet ring or colloid type are extremely rare. More than 25 per cent of all cases show *metastases* at the time of operation. These occur by way of the nerves, the lymphatics, the blood vessels, and direct extension. In approximately the order of frequency, the organs and tissues involved are: mesenteric lymph nodes, peritoneum, liver, lungs, supraclavicular lymph nodes, long bones and any other site. The *operative mortality* varies from 22 to 44 per cent and the *five year cure* rate ranges from 0 to 12 per cent. The average duration of life following the onset of symptoms is six to fourteen months.

Carcinoid tumors.—These have *also* been called argentaffinomas, chromaffinomas, paragangliomas and primary carcinomas. They arise from the argentaffine cells that are located in the depths of the crypts of Lieberkuhn. These tumors are found anywhere in the *gastrointestinal* tract but most of them are located either in the



FIG 285 —Polypoid carcinoma of the jejunum.

appendix or in the terminal ileum. They comprise about one-quarter of all malignant neoplasms of the small intestine. They have no predilection for either sex and are usually discovered in the sixth decade of life. The *tumors* may be single or multiple, are found anywhere along the circumference of the gut and usually measure from 0.2 to 4 cm. in diameter. As a rule, they grow sub-mucosally, are firm and sharply circumscribed, usually push into the lumen to produce polypoid masses, less often grow outwardly into the muscle, and are frequently accompanied by fibrosis. The mucosal surface is intact, atrophic or ulcerated; the serosa is often kinked and the bowel angulated, and the cut surface is orange to yellow in color. *Histologically*, they are composed of sheets, nests or cords of polygonal, uniform but ill-defined cells. The cytoplasm is moderately eosinophilic, granular or minutely vacuolated and the nuclei are central, round or oval and evenly stained. Less often carcinoids tend to form glands or pseudoglands wherein the cells

are columnar or cuboidal and the nuclei are basally situated (Fig 286) In pseudoglands there are no true lumens for the central portion is filled with homogeneously eosinophilic material In all cases, the cells are identified by silver staining which discloses numerous densely packed brown to black cytoplasmic granules Although carcinoids are generally considered as benign, it is reported that 25 per cent of those found in the small bowel metastasize Secondary growths are found in the regional nodes, mesenteric fat, liver, peritoneum and retroperitoneal nodes Treatment is radical excision of all tumors The prognosis even in cases with metastases is relatively good for growth is slow

Neurofibrosarcoma—Neurofibrosarcoma of the small intestine exists in conjunction with neurofibromas disseminated throughout the body or as a solitary lesion It arises from the sheaths of the



FIG 286—Carcinoid of the intestine showing glandular formation $\times 100$

nerves that are located in the muscle coats Growth is usually towards the serosa, where the tumor becomes pedunculated and often adherent to surrounding organs, while less frequently it is towards the lumen The tumors are encapsulated, firm, greyish white or vascular, and tend to undergo central necrosis, hemorrhage and liquefaction, leaving only a peripheral shell of solid tissue Histologically, they consist of large spindle-shaped cells with elongated deeply stained nuclei that are arranged in whorls and interlacing bundles As a rule, there is some palisading of the nuclei although this sometimes is not pronounced Frequently, the tumors are localized to the bowel despite their large size Metastases first occur in the regional lymph nodes

Leiomyosarcomas—These are single or multiple intramural tumors that start in the smooth muscle of the gut and protrude into the lumen or bulge towards the serosa They produce symptoms by occluding the lumen, angulating the bowel or by causing ulceration of the mucosa and hemorrhage Grossly, they are sharply

circumscribed, moderately firm or soft, light greyish brown or grey and measure to 15 cm. or more in diameter. *Histologically*, some resemble smooth muscle and these consist of interlacing bundles of elongated cells with fibrillar cytoplasm and deeply stained oval or more spindle-shaped nuclei, while others consist of more irregular polyhedral cells. Mitoses and multinucleated giant cells may be numerous. These tumors are usually of low grade malignancy and resection is therefore often successful.

Lymphoblastomas.—Lymphoblastomas in the small intestine as in other organs constitute chiefly lymphosarcoma, reticulum cell sarcoma and Hodgkin's disease. The latter is the least common. These lesions may be *primary* in the bowel or they may be *part of a generalized disease*. They affect three males to every female, and although they are found at all ages they are most common in the fourth and fifth decades. They comprise from one-third to one-

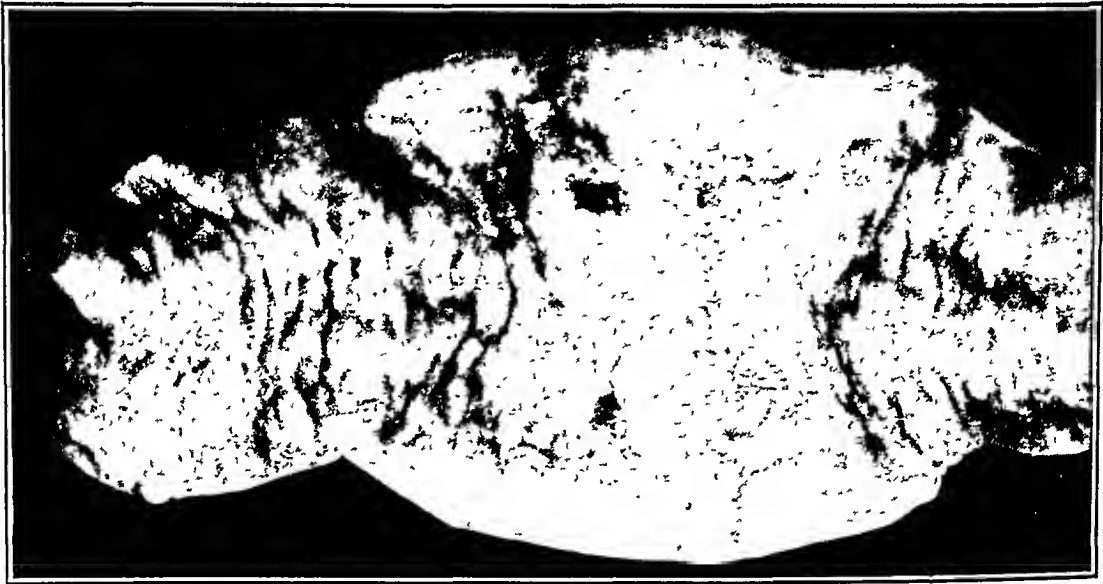


FIG. 287.—Lymphosarcoma of the ileum.

half of all malignant lesions of the small intestine and are most common in the lower ileum. The *lesions* originate in the lymph follicles or Peyer's patches, are frequently multiple, and usually do not measure more than 5 cm. in greatest diameter. They grow either as polypoid masses that project into the lumen or as cuff-like uniform thickenings that infiltrate the wall diffusely (Fig. 287). The mucosa is intact until late in the disease when it becomes ischemic and necrotic; the lumen is usually not greatly constricted (obstruction results from contraction of the bowel proximal to the tumor and from paralysis of the involved segment), and the tumors on section appear diffusely light grey. *Histologically*, they do not differ from other lymphoblastomas which are described in Chapter XVI. Of those primary in the intestine, spread takes place by way of the lymphatics to the regional lymph nodes and by way of the blood stream to distant organs and tissues. *Treatment* consists of surgical extirpation followed by irradiation therapy. The *prognosis* is not good.

Secondary Neoplasms—Secondary neoplasms of the small intestine are relatively common. They reach the small bowel (1) by direct extension from contiguous tumors, as for example, involvement of the duodenum by carcinoma of the head of the pancreas, or (2) by way of the lymphatics and blood vessels from distant foci. The latter includes carcinoma of the stomach, pancreas, uterus, colon, liver, gall bladder, breast, testicles and other sites. Of particular interest, perhaps, is *melanoblastoma*. Although this tumor has been described as occasionally arising in the small bowel, it is probable that this assumption is incorrect and that all such tumors are metastatic. The latter contention is supported by the fact that melanoblasts have never been demonstrated in the wall of the small bowel.

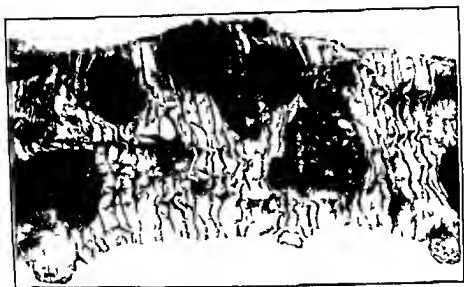


FIG. 288—Metastatic melanoblastoma of the small intestine.

When a melanoblastoma is encountered in the small intestine it, therefore, behooves one to look for a primary focus elsewhere. Secondary tumors of the small bowel are *single*, if they develop as extension from adjacent tumors, or, as a rule, *multiple* if they are metastatic (Fig. 288). They are initially submucosal but as they enlarge they form intraluminal nodules with sessile or pedunculated bases and intact or ulcerated mucosal surfaces. They vary in size from less than a millimeter to 3 or 4 cm in diameter. *Histologically*, they resemble the parent tumor. They produce *symptoms* by impinging directly upon the lumen or by producing intussusception. The *prognosis* in secondary tumors that arise as direct extensions is not necessarily hopeless, while fatalities in metastatic growths are 100 per cent.

Mechanical Disturbances—These may be briefly considered under the following headings: intussusception, volvulus, occlusions of mesenteric vessels, meconium ileus, paralytic ileus, rupture, foreign bodies and obstruction. Hernias are discussed in the chapter on the peritoneum.

Intussusception.—This is a telescoping of one segment of bowel into another. By far the greatest number of cases are *isoperistaltic* or descending and these are ordinarily divided into primary and secondary. *Primary* intussusceptions are those in which no definite cause is demonstrable. Theoretically, however, they are attributed to excessive mobility of the cecum and ascending colon, hyperplasia of lymphoid tissue in the ileum, protrusion of the ileo-cecal valve into the large bowel, upset of normal muscular coordination, in-coordination of the autonomic nervous system, dietary indiscretions and excessive purgation. This type of invagination is practically confined to infants. *Secondary* intussusception is the type usually seen in adults and is caused by tumors, inflammations such as typhoid, dysentery and tuberculosis, and Meckel's diverticulum. Retrograde or *ascending intussusception* accounts for only 0.5 per cent of all invaginations. It results from antiperistalsis and is due

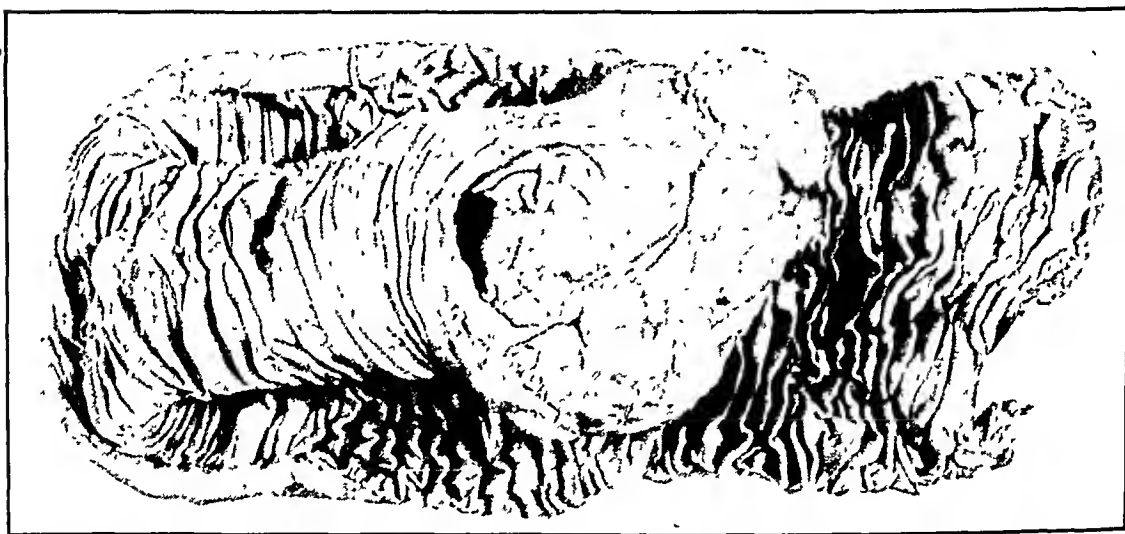


FIG. 289 —Intussusception of the small intestine caused by a polypoid carcinoma
The intussuscipiens has been incised

to chemical irritants, inflammations, mechanical obstruction and neuropathic states. This type is found anywhere from the sigmoid to the stomach and includes jejunal invagination into the stomach by way of a gastroenterostomy. Eighty per cent of all intussusceptions occur in children under two years of age, and males are affected twice as frequently as females. The cardinal *manifestations* in acute types are periodic attacks of colicky abdominal pain, vomiting, mucus and blood in the stools and a palpable abdominal mass between attacks. In chronic types, the chief symptom is repeated colicky pain in the abdomen. Intussusception occurs anywhere in the gastro-intestinal tract, but is most common in the *ileo-cecal* region. The receiving loop of bowel consists of one layer and is called the *intussuscipiens*, while the advancing segment consists of two layers of gut and is called the *intussusceptum* (Fig. 289). The chief *pathologic* changes exist in the latter in the form of edema, congestion, extravasation of blood, excess secretion of mucus, ulceration

and gangrene. The intussusceptions become congested, covered with fibrin and occasionally perforates. *Treatment* of intussusception is operative. The invagination is reduced and the cause removed. If reduction is impossible the involved segment must be resected. The *mortality* varies from 4.9 to 32.5 per cent and depends upon the duration of symptoms before operation and the extent of the operative procedure. The *causes of death* are shock, toxemia and dehydration.

Volvulus—This is a twisting or knotting of the bowel that usually results in obstruction. The *cause* is fixation of one portion of the gut and free movement of another. These conditions are found (1) in such congenital lesions as Meckel's diverticulum, mobile ileum and cecum when the posterior mesentery is unattached, and exomphalos, and (2) in such acquired lesions as adhesions, tumors, mesenteric cysts, and intestinal gall stones. Ingestion of coarse food is said to play an etiologic role. Volvulus is found at all ages with a peak incidence in the third decade, and affects males more frequently than females. Two-thirds of the lesions are located in the small bowel while most of the rest are found in the sigmoid colon and cecum. The *rotation* is clockwise and varies from 90° to 720° . The tightness of the twist is more important than the degree of rotation or the number of coils. The *pathologic* changes consist of obstruction with collection of gas and fluid in the involved segment, venous and then arterial occlusion, infarction of the wall, gangrene, perforation and peritonitis. *Treatment* is laparotomy, detorsion and correction of the cause.

Occlusions of mesenteric vessels—These disturbances are more common in the veins than in the arteries. The *causes of venous* obstruction are thrombosis resulting from lesions in organs that drain into the portal vein such as appendicitis and strangulated hernias, from trauma, and from increased portal pressure. The *causes of arterial* occlusions are embolism to the superior mesenteric artery from vegetations in the left side of the heart, and less frequently, from thrombosis caused by arteriosclerosis or following lumbar sympathectomy. The condition is rare in children, reaches its peak in the fifth decade, and affects two males to every female. Occlusion of the *superior mesenteric artery* produces anoxia and spastic contraction of the bowel. The intramural vessels are compressed, the capillary blood is drained off, and the bowel is firm and white. The ensuing fatigue causes relaxation resulting in negative pressure in the vessels and a reflux of blood from the veins and collateral arteries. This produces hemorrhagic infarction. Occlusion of the *mesenteric veins* eventuates in an immediate infarction and relaxation of the bowel. In either case, there subsequently occur edema, thickening, gangrene and even perforation of the wall, and escape of blood tinged fluid into the lumen of the bowel and the peritoneal cavity. After twelve hours, there develops a frank peritonitis. *Symptoms* are those of intestinal obstruction produced not by occlusion of the lumen but by paralysis of the intestinal wall. The only effective *treatment* is surgical resection of the involved segment. The *mortality* is 90 per cent.

Meconium ileus.—Meconium ileus is a term used to designate inspissation of meconium in the terminal ileum of a newborn infant with resultant intestinal obstruction. The cast consists of mucus, epithelial cells, and calcium carbonate. Two factors are probably responsible for the condition; (1) a deficiency or absence of pancreatic secretion for it has been shown that the duct of Wirsung may be stenotic and (2) spasm of the terminal ileum which prevents normal evacuation of meconium. Stasis and dehydration then result in inspissation of the contents.

Paralytic ileus.—Paralytic ileus has also been *called* inhibition ileus and adynamic obstruction. The condition consists of a rapid dilatation of the entire intestine (to varying degrees) and is occasioned not by a paralysis of the vagus nerves but by an over-activity of the sympathetic nerves. The *causes* are (1) infection as peritonitis and retroperitoneal inflammations, (2) trauma as after abdominal operations, blow to the abdomen, fractured ribs and thoracoplasty, (3) directly nervous, as after ether anesthesia and spinal cord injuries and (4) miscellaneous as strangulated hernias, renal or gall bladder colic, twisted ovarian cyst and torsion of the spermatic cord. *Symptoms* are those of intestinal obstruction. In fully developed cases of non-inflammatory origin, the *bowel* is dilated with fluid and air, the wall is thin and dusky, and the serosa is smooth. In cases with peritonitis, the serosa is, of course, covered with an exudate and the peritoneal cavity contains pus. *Treatment* is (1) decompression by intestinal suction sometimes augmented by stimulants such as pituitary extract and prostigmine, and (2) attention to the causative factor.

Rupture.—Rupture of the intestines may be produced by *penetrating* or *non-penetrating* injuries. The mechanism involved in the former is obvious, while that in the latter probably consists of (1) compression of the bowel by the force against the spine or pelvis, (2) tearing when the force is applied at an angle and (3) bursting injuries as compressed air in the anal canal. Distention of the bowel with food and hernias are predisposing causes, while the forces usually consist of blows by blunt objects, falls, automobile accidents and kicks. In penetrating wounds, any portion of the gastrointestinal tract may be involved, while in non-penetrating trauma, the ileum is most commonly affected. *Symptoms* and *signs* may be immediate or delayed. They include abdominal pain and tenderness and a rapid pulse. Later, they are those of acute peritonitis. *Treatment* consists of laparotomy and simple closure or resection of the bowel. The *prognosis* depends upon the promptness of diagnosis which is often extremely difficult. The mortality rate is 50 per cent.

Foreign bodies.—They are uncommon in the small intestine for most objects that pass through the stomach also pass through this portion of the gut. In patients with gastroenterostomy, bezoars have been known to pass through the gastric ostium into the jejunum. Gall stones eroding from the gall bladder or common bile duct, may become lodged in the lower ileum, and enteroliths composed of a nucleus of epithelium or other material surrounded

by mineral salts, may form at the same site. Finally, intestinal diverticula may occasionally trap smaller objects.

Obstruction—Obstruction of the small intestine is caused by numerous pathologic conditions. A recapitulation of these is virtually a summary of diseases of this portion of the bowel. In outline form they include (1) *congenital anomalies* such as umbilical hernia, stenosis, atresia, diaphragms, duplications and cysts, mesenteric cysts, Meckel's diverticulum or other abnormalities of the vitelline duct and annular pancreas, (2) *inflammations* such as acute phlegmonous enteritis, fibrosis following duodenal ulcer, syphilis, tuberculosis, regional enteritis and peritoneal adhesions, (3) *tumors* both benign and malignant and (4) *mechanical disturbances* such as intussusception, volvulus, hernias, occlusions of mesenteric vessels, paralytic ileus, spastic ileus and foreign bodies including gall stones, enteroliths, iscaris lumbricoides, inspissated meconium and bezoirs.

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Chapter XII

APPENDIX

EMBRYOLOGY

AS ALREADY stated, the appendix arises as an evagination of the distal end of the cecal bulge. Lengthening rapidly at first, it soon lags behind the development of the rest of the bowel and forms the organ as we know it.

ANATOMY

The appendix is a long narrow worm-shaped tube (hence also called the vermiform process) that measures from 2 to 20 cm. in length and as much as 0.5 cm. in transverse diameter. Originally, the base is attached to the apex of the cecum but with growth, it is shifted medially and posteriorly. The usual *positions* of the organ are: hanging over the brim of the pelvis, lying below the colon and cecum, or directed behind the cecum and ascending colon. Rarely, it lies anterior or posterior to the terminal portion of the ileum. A fold of peritoneum (the mesentery of the appendix) connects it with



FIG. 290.—Normal appendix. x 25.

the mesentery of the ileum. The *blood supply* comes from the appendicular artery which arises from the ileocolic branch of the superior mesenteric; the *veins* drain into the superior mesenteric vein, and the *lymphatics* empty into the ileocolic lymph nodes.

Histologically, the triangular lumen contains dead cells, fecal material and other detritus but it may be collapsed; the mucosa consists of cells similar to those described in the small intestine with, however, a relative increase in argentaffine cells; the tunica propria and part of the submucosa contain lymphoid follicles which normally increase in number and size until the tenth year, after which they

gradually disappear, the muscularis mucosa is poorly developed, the submucosa contains connective tissue, fat, blood vessels, lymphatics and nerves, the muscle is formed of two layers, and the serosa is composed of connective tissue covered with mesothelial cells (Fig. 290)

PATHOLOGY

Congenital Anomalies—If the wide variations in size and the different positions already enumerated are held as normal then developmental abnormalities of the appendix must be considered as rare. There have been described an *aplasia*, *duplication* (partial or complete associated with a single or double cecum), *diverticulosis*, a *left-sided* position in cases with situs inversus, and *congenital fibrous bands* often producing kinks of the organ. In the presence of inflammation, a left-sided appendix offers difficulty in diagnosis and congenital bands with resultant kinks predispose to infection. Otherwise, the anomalies mentioned are of little practical significance.

Inflammations—**Non-specific Inflammations**—Non-specific inflammations of the appendix may be variously classified, but merely affixing adjectives does not necessarily clarify the understanding of either the pathological process or the clinical course. The disease will therefore be considered under two headings—acute and chronic appendicitis.

Acute Appendicitis—This is the most frequent lesion that a surgeon is called upon to treat. Its causes may be divided into (1) precipitating and (2) predisposing. The *precipitating* factor is bacterial. The organisms almost always reach the appendix from the lumen and, therefore, usually consist of the colon group and streptococci. Much less frequently (and some authors say rarely if ever) are they carried in hematogenously and also rarely, is the appendix involved by extension from neighboring organs. The *predisposing* factor is obstruction to the lumen which may be caused by fecoliths, fibrosis of the wall at the base, foreign bodies, swelling of the lymphoid apparatus, worms, spasm of the muscle at the base, kinks, twists, adhesive serosal bands and, less commonly, by tumors. The relationship of these factors, and, therefore, the *pathogenesis*, may be outlined as follows. When the lumen is occluded the epithelial cells continue to secrete, the intraluminal pressure is increased until it equals or surpasses the blood pressure, this decreases the blood supply which in turn produces anoxia, degeneration and even focal necrosis of the tissues, and these changes finally pave the way for invasion by the organisms that are usually found within the lumen.

Acute appendicitis occurs at all ages from infancy to senility with, however, a peak incidence in the second and third decades, and with only 2 per cent beyond the age of sixty years. Males are affected more often than females. There is no particular relation to seasons or to upper respiratory infections. The characteristic symptoms and signs are as follows. (1) Pain. This begins around the um-

Chapter XII

APPENDIX

EMBRYOLOGY

AS ALREADY stated, the appendix arises as an evagination of the distal end of the cecal bulge. Lengthening rapidly at first, it soon lags behind the development of the rest of the bowel and forms the organ as we know it.

ANATOMY

The appendix is a long narrow worm-shaped tube (hence also called the vermiform process) that measures from 2 to 20 cm. in length and as much as 0.5 cm. in transverse diameter. Originally, the base is attached to the apex of the cecum but with growth, it is shifted medially and posteriorly. The usual *positions* of the organ are: hanging over the brim of the pelvis, lying below the colon and cecum, or directed behind the cecum and ascending colon. Rarely, it lies anterior or posterior to the terminal portion of the ileum. A fold of peritoneum (the mesentery of the appendix) connects it with



FIG 290 —Normal appendix. x 25.

the mesentery of the ileum. The *blood supply* comes from the appendicular artery which arises from the ileocolic branch of the superior mesenteric; the *veins* drain into the superior mesenteric vein, and the *lymphatics* empty into the ileocolic lymph nodes.

Histologically, the triangular lumen contains dead cells, fecal material and other detritus but it may be collapsed; the mucosa consists of cells similar to those described in the small intestine with, however, a relative increase in argentaffine cells; the tunica propria and part of the submucosa contain lymphoid follicles which normally increase in number and size until the tenth year, after which they

appendicitis Progression of the inflammatory process results in a thick, dull grey, diffusely pus and fibrin covered serosa, to which may be adherent the omentum or other organs and tissues (Fig. 291). The serosal congestion thus becomes less apparent, the wall is usually thin and soaked with purulent material, the mucosa is ulcerated, the lumen is still larger and filled with pus, and the mesentery is thick, edematous and friable. In this stage, the process may be labelled *acute suppurative appendicitis*. Further advancement of the inflammation results in complete death of a portion of the organ or of the entire organ. The external surface is of a variegated grey, red and black color and is covered with irregular plaques of fibrinopurulent exudate. The wall is thin, friable and extremely vulnerable so that perforations in the blackened areas are frequent (Fig. 292). Its inner surface and the mucosa are completely ulcerated and the lumen is filled with grey pink or hemorrhagic pus, necrotic tissue and fecal material. This is the *gangrenous and perforated* stage of the disease. *Histologically*, the earliest changes consist of congestion of the mucosal and submucosal capillaries in which there is both an increase in number and a margin-



FIG. 292—Perforated gangrenous appendicitis

ation of leukocytes. Simultaneously, there is transudation of plasma and a beginning extravasation of neutrophils into the surrounding tissue. The mucosal glands disclose an increased secretion of mucus and a compression of the epithelial cells. The organisms extending along the penetrating vessels to the serosa bring about a spread and an intensification of the inflammatory process. Neutrophils and to a lesser degree eosinophils, infiltrate all the layers in great numbers, the normal landmarks gradually become obliterated, the mucosa ulcerates, and the underlying tissue becomes completely destroyed, necrotic and liquefied (Fig. 293).

Of course, not every organ or all parts of the same organ disclose all the changes enumerated for at any stage the infection may be interrupted, either by removal of the appendix or by death of the organisms, followed by a repair of the damage. Thus, if the inflammatory process is arrested before there is tissue destruction, resolution may take place in the usual manner resulting in complete restoration of the organ to normal. Frequently, however, the infection is more severe. The destroyed portions are replaced first with granulations and then with dense sclerotic connective tissue, resulting in fibrosis of the submucosa and mucosa and in complete

bilicus, is localized to the right lower quadrant when the peri-appendical tissue is involved and becomes diffuse when generalized peritonitis develops. (2) Nausea and vomiting becoming manifest subsequent to the onset of pain. (3) Fever usually of 100°F. to 101°F. until peritonitis supervenes, when it is, as a rule, over 102°F. (4) Abdominal tenderness which is usually maximum in the right lower quadrant. In addition, the following may also be present: spasm of the rectus muscles, rectal tenderness, leukocytosis with a relative increase of neutrophils, constipation, diarrhea and dysuria. Symptoms and signs are not necessarily characteristic in infants and young children, where the information is obtained from a second party, nor are they always characteristic in people over sixty years of age. In the latter, there may be only lower abdominal pain with



FIG. 291 —Acute suppurative appendicitis The serosa is covered with pus and the tip is surrounded by a portion of the omentum.

local tenderness over McBurney's point. Leukocytosis may not be present and there is often no fever, nausea or vomiting. The reasons advanced for these minimal manifestations are a decreased sensitivity to pain and an inclination of older people to conceal illness.

Early in the course of the disease, the appendix may show no grossly detectable changes. The first alterations consist of an increase in size of the organ manifested by a smoothing out or rounding off of the external angulations. The serosa is dull grey; the vessels are congested and prominent; there are various degrees of perivascular deposition of pus; the wall is thick, rigid and firm; the mucosa is still intact; the lumen is usually somewhat dilated, and it contains a fecolith, debris, mucus or pus. If a specific name were to be attached to such an organ, it might be called simple *acute*

below the liver, below the diaphragm, between the angle of the ileum and the ascending colon and within the pelvis. *Intestinal obstruction* occurs as a complication of acute appendicitis in 6 per cent of all cases. Early in the disease, it is, as a rule, an accompaniment of generalized peritonitis, whereas in the absence of peritonitis, it is due to adhesions. In the early postoperative period, these are fibrous and not of serious import for the obstruction (which is also due in part to adynamic ileus) can be relieved by gastrointestinal suction and a second operation can thus be avoided. Later, adhesions are fibrous and occlusion of the bowel can be relieved only by lysis.

The *diagnosis of acute appendicitis* is difficult in infancy and in old age, but between those two extremes it is, as a rule, readily established. In typical cases, the cardinal manifestations are abdominal pain, nausea and vomiting, fever, abdominal tenderness and frequently leukocytosis. In atypical cases, pain may be the only symptom and tenderness the only sign. *Treatment* consists of immediate appendectomy when the organ is acutely inflamed and unruptured, or when it is inflamed and ruptured, but when there is no localization of the inflammatory process. If the appendix is perforated and the infection is localized, the consensus is that operation should be delayed. Meanwhile, the patient should be treated by gastrointestinal decompression, no food or fluids by mouth, morphine, chemotherapeutic drugs, antibiotics and oxygen. Abscesses often resorb spontaneously, otherwise they should be drained. Aside from the abdominal complications already mentioned the *causes of death* are attributable to pulmonary embolism, pneumonia and other unrelated disease processes. The *mortality* is influenced by the duration of symptoms before operation, the complications, the type of treatment, the postoperative care and the age of the patient. In the aged, the over-all death rate is about 25 per cent, in unperforated acute inflammations, it is 0 to 1.53 per cent, in perforated appendices, it is 1.75 to 2.99 per cent, in the presence of an abscess, it is about 3 per cent, and in the presence of peritonitis, it is about 13 per cent.

Chronic Appendicitis—This is a *clinical term* used to connote recurrent pain in the right lower quadrant of the abdomen. It is thought to be due to *intermittent attacks of acute appendicitis*. *Pathologically*, it should mean an infiltration of the appendix with plasma cells, monocytes and lymphocytes. Actually, however, such a histologic picture is rarely seen. Instead one often finds the organ to be normal or less frequently the seat of adhesions, fecoliths, foreign bodies, kinks, twists, increase of fibrous tissue, hyperplasia of lymph follicles and complete fibrous obliteration of the lumen with a proliferation of the nerve endings to produce what appears like an amputation neuroma. In an attempt to correlate the clinical findings and the microscopic appearances, some of the *terms* that have been employed are chronic lymphoid appendicitis, scarring of the appendix, lymphoid hyperplasia, neuroma of the appendix and neurogenic appendix. The condition is encountered more frequently in adults with a slight preponderance in males. In addition

obliteration of the lumen. This may be considered as a successful termination.

In other cases, however, where the organisms overwhelm the host, the infection proceeds, resulting in a series of *complications*. These consist of peritonitis, abscess, intestinal obstruction, pylephlebitis and fistula. *Pylephlebitis* is considered in connection with the liver and *fistula* is discussed at the end of this chapter under mechanical disturbances. *Peritonitis* may be *focal* or *generalized*. The former is present to some degree in every case of acute appendicitis as soon as the infection reaches the serosa. In most cases, this is not too serious for it resolves or at the most results in focal adhesions or abscess. *Generalized* peritonitis, however, is serious, and accounts for 95 per cent of the deaths. It usually follows a sudden perforation of the appendix accompanying which there is flooding



FIG 293 —Acute suppurative appendicitis. The lumen is dilated and filled with a fecolith; the mucosa is denuded, and the wall is edematous, congested and diffusely permeated with neutrophils. $\times 37.5$.

of the peritoneal cavity with a large amount of contaminated material. This is particularly true of the disease in children under two years of age when the omentum is less effective in localizing the infection. In other cases, diffuse peritonitis is due to contamination of the peritoneum at the time of operation by transperitoneal drainage of an abscess, by breaking up of newly formed adhesions and by failing to drain the peritoneal cavity. The incidence of this complication is recorded as varying from 14.9 to 22.2 per cent of all cases of acute appendicitis. *Abscesses* are reported as occurring from 10 to 56 per cent of all cases. They arise as a successful termination of a generalized peritonitis, following a perforation and, least frequently, after a simple suppurative infection. In all cases, localization is assisted by the omentum and various regional structures and organs. Abscesses are usually single but they may be multiple, and they vary in size from a few millimeters to 15 or 20 cm. in diameter. They are located around the cecum, behind the cecum,

than males. Some are asymptomatic while others produce symptoms of acute or "chronic" appendicitis. These are due respectively to an actual accompanying infection or to obstruction of the lumen.

In three-quarters of the cases carcinoids are located in the distal third of the appendix where they, as a rule, produce a bulbous swelling. The serosa is generally smooth, but it may be roughened by adhesions and knuckled or knicked. On section, the tumors usually consist of single submucosal nodules that measure 0.5 to 1.0 cm in diameter. Sometimes, however, they are annular and rarely, do they become large enough to be palpated through the abdominal wall. They are sharply demarcated but not encapsulated, and because of the deposition of cholesterol and lecithin they present the usual yellowish color. *Histologically*, as already de-

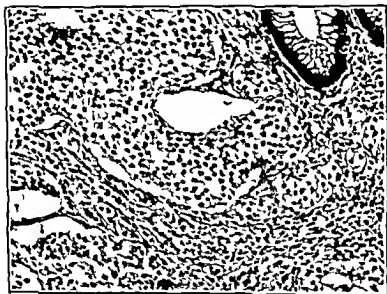


FIG. 294.—Carcinoid of the appendix. The cells are uniform, finely vacuolated and arranged in nests and cords. $\times 100$.

scribed in connection with the small intestine, they usually consist of nests, strands or cords of uniform appearing cells supported by a stroma of dense fibrous tissue (Fig. 294). Less commonly they form glands, pseudoglands or rosettes.

Treatment consists of appendectomy. In fact, the lesion is usually not discovered until histologic sections are studied. All carcinoid tumors are potentially cancerous, although in the appendix a malignant change is said to occur in only 5 per cent of the cases. Even in these cases metastases ordinarily occur to the mesenteric lymph nodes and rarely to the liver. The prognosis is, therefore, good.

Carcinoma—Carcinoma of the appendix is rare. The incidence, however, is difficult to determine, because in many scientific papers on the subject a distinction between carcinoid and carcinoma is still not clearly made. My own experience consists of three cases. In

to the pain, there may be tenderness on deep palpation in the right lower quadrant, nausea and vomiting, but there is rarely muscle rigidity, fever or leukocytosis. The patients are usually subjected to appendectomy lest something more serious befalls them. Such *treatment* renders partial or complete relief of symptoms in about three-quarters of the cases—in those in whom the manifestations are of recent origin, in whom the pain and tenderness are localized and in whom some pathologic change is found in the appendix. The rest of the cases are unimproved or are actually made worse.

Specific Inflammations.—Granulomatous lesions of the appendix are extremely rare. The only two worthy of mention are *actinomycosis* and tuberculosis. The latter usually occurs as a direct extension from *tuberculous* peritonitis and salpingitis, and less frequently as a hematogenous spread in cases of pulmonary or miliary tuberculosis.

Tumors.—Although theoretically any of the tissues that compose the appendix can give use to benign and malignant neoplasms, the different types and numbers of tumors that have actually been described are few. - From the epithelium there have been recorded an adenoma, carcinoid and carcinoma; from lymphoid tissue, a giant follicular lymphoblastoma and lymphosarcoma; from connective tissue, a fibrosarcoma and myxosarcoma; from vessels, an endothelial sarcoma; from nerves, a neuroma and Schwannoma, and from muscle, a leiomyosarcoma. The only lesions that need be briefly described here are adenoma, carcinoid, carcinoma and lymphosarcoma.

Adenoma.—Adenomas are infrequently recorded, probably because it is the custom in many laboratories to omit longitudinal incision of the appendix and careful examination of the mucosa. Of the recorded cases, there has been no predilection for either sex, and most of the patients have been under the age of forty years. It is said that the disease is familial and that it also occurs as a reactive hyperplasia to prolonged inflammation. *Symptoms* are not directly attributable to the adenomas as such, but are those of their complications which consist of acute appendicitis and intussusception. Otherwise, except for vague abdominal pain, adenomas are asymptomatic. *Grossly*, they appear as single or multiple, pedunculated or sessile, soft mucosal masses that usually measure from 0.5 to 3.7 cm. in length. *Histologically*, they are composed of connective tissue stalks covered with a single layer or glands of columnar or cuboidal cells among which there is a preponderance of mucous secreting goblet cells. A cancerous transformation has never been recorded.

Carcinoid tumors.—These occur more frequently in the appendix than in any other portion of the gastrointestinal tract. They are twice as common here as they are in the small intestine, and they are present in from 0.2 to 0.5 per cent of all removed appendices. As in other portions of the intestinal tract, they arise from argentaffine cells which are particularly numerous in the appendix. They are found at all ages, from childhood to senility with a preponderance in the third decade, and affect females somewhat more frequently

than males. Some are asymptomatic while others produce *symptoms* of acute or "chronic" appendicitis. These are due respectively to an actual accompanying infection or to obstruction of the lumen.

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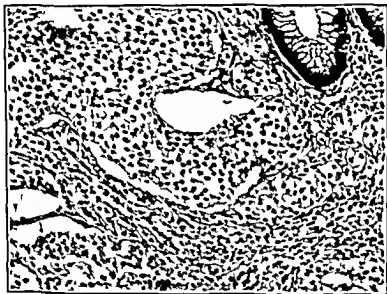


FIG. 294.—Carcinoid of the appendix. The cells are uniform, finely vacuolated and arranged in nests and cords. $\times 100$

scribed in connection with the small intestine, they usually consist of nests, strands or cords of uniform appearing cells supported by a stroma of dense fibrous tissue (Fig. 294). Less commonly they form glands, pseudoglands or rosettes.

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contrast to carcinoids, the patients are usually in the fifth or sixth decades of life. Females are affected three times as frequently as males, and *symptoms* are similar to those accompanying carcinoids. Carcinomas are almost always located in the proximal one-half of the appendix. They arise in the mucosa, may reach large dimensions and may even produce a palpable mass. *Histologically*, they are similar to carcinoma of the rest of the gastro-intestinal tract. Most frequently, they are composed of columnar cells in adenomatous formation and possess a strong tendency to undergo a mucinous transformation. Growth and *metastases* are the same as in carcinoma of the small intestine. Because, however, they produce symptoms sooner, these tumors are removed earlier and the *prognosis* is, therefore, somewhat better.

Lymphosarcoma.—Lymphosarcoma of the appendix is also rare. It has been described both as a primary process and as part of a disseminated disease. It occurs at all ages and affects males and

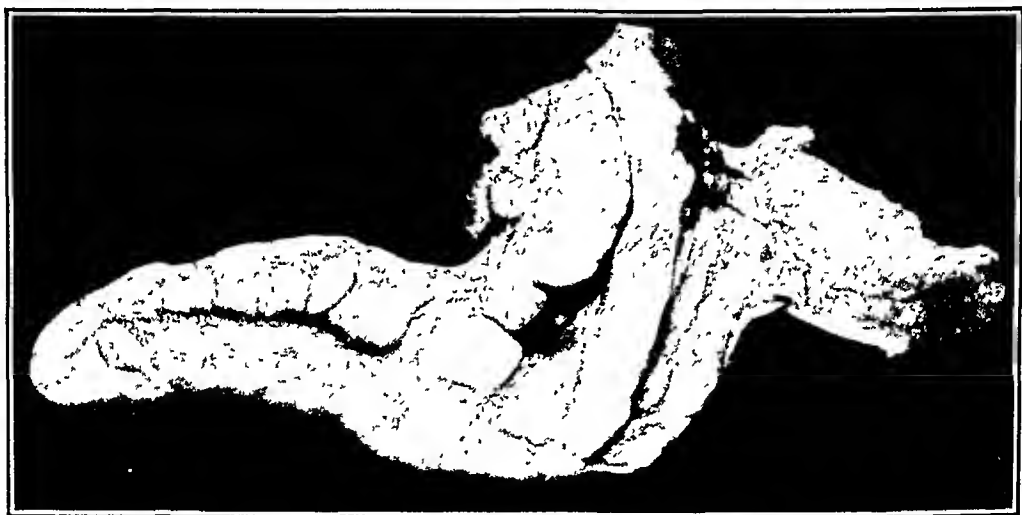


FIG 295.—Lymphosarcoma of the appendix.

females with equal frequency. When *symptoms* are present they consist of a dull aching or recurrent colicky pain in the right lower quadrant of the abdomen, and less frequently, of other manifestations of appendicitis. Sometimes, a tumor is palpable beneath McBurney's point. *Grossly*, the appendix is considerably enlarged, tense and firm (Fig. 295). The serosa is smooth and grey; the wall is greatly thickened by light greyish white homogeneous tissue which may accentuate or completely obliterate the normal markings; the mucosa is thick and frequently appears intact, and the lumen although encroached upon is, as a rule, empty. *Histologically*, most or all of the normal glandular pattern of the mucosa gradually disappears and the entire wall is diffusely and completely infiltrated with lymphocytes or lymphoblasts. *Treatment*, albeit usually under a mistaken diagnosis of inflammation, is appendectomy. This should be followed by irradiation therapy. The *prognosis*, however, is poor for very few of the patients survive more than twelve months after the disease is discovered.

Mechanical Disturbances—Under this caption may be considered mucocele, concretions and calculi, worm infestations, trauma, fecal fistula and intussusception

Mucocele—Mucocele of the appendix signifies an accumulation of mucoid material within the lumen. It occurs at any age but is most frequent in the fifth decade, and it predominates in females. The usual cause is considered to be an obstruction to the lumen in the presence of relatively sterile contents. The disease can be produced at will in rabbits by first irrigating the lumen and then ligating the base of the appendix. If, however, the irrigation is omitted, gangrenous appendicitis rapidly follows. In addition to the above explanation, some authors maintain that the process in a minority of cases is a low grade adenocarcinoma of the appendix.



FIG. 296.—Mucocele of the appendix.

They reason that if the latter appendix ruptures the contents continue to grow in the abdominal cavity and produce pseudomyxoma of the peritoneum, while if the simply obstructed organ perforates there are no dire consequences. It is probable that both views are correct. There are no characteristic *symptoms* and *signs*. Some patients complain of pain in the right lower quadrant of the abdomen that is neither very severe nor well-localized. There may also be nausea, a palpable abdominal mass and manifestations of intestinal obstruction.

Grossly, the appendix may be normal in size and configuration or it may be globular, oval or elongated and measure as much as 20 cm. in diameter (Fig. 296). The serosa is smooth and glistening. As the mass increases in size the wall becomes correspondingly thinner and weaker until diverticula form or rupture occurs. The inner surface is smooth in some cases, while in others it is rough and covered with small papillary excrescences. Early, the contents are thin, clear or turbid, and sticky. As the water is absorbed they

become thicker and more gelatinous, whereas in the presence of a low grade infection they tend to become opaque and inspissated. Clinically, the material shows all gradations from mucin to pseudomucin. *Histologically*, the appendix discloses initially a normal or hyperplastic mucosa in which the cells are cuboidal or columnar and are distended with secretion. In time, however, the epithelium undergoes pressure atrophy and partly or almost completely disappears. Simultaneously, as the organ becomes distended, the layers of the wall gradually lose their identity until ultimately they are replaced with fibrous connective tissue.

The *diagnosis* of mucocele is seldom made clinically. *Treatment* consists of appendectomy. The *complications* are (1) rupture resulting in pseudomyxoma of the peritoneum and intestinal obstruction, and (2) carcinoma which may be the original cause of the obstruction. The *prognosis* is good if the contents are confined to the appendix, but it is poor if they are disseminated throughout the peritoneal cavity.

Concretions and Calculi.—Concretions and calculi of the appendix are related. *Concretions* are commonly known as fecoliths and are found in three-quarters of all surgically removed appendices. They are single or multiple, round, oval or elongated structures composed of inspissated fecal material that becomes adapted to the lumen of the appendix. Some are firm, others are soft but they do not contain calcium. Their chief importance lies in the fact that they occlude the lumen and, therefore, predispose to appendicitis. *Calculi* on the other hand are rare. They are single, roughly globular masses that distend the lumen and measure as much as 4 cm. in diameter. They contain calcium and are, therefore, radio-opaque. The genesis of both fecoliths and calculi is essentially the same. Normally fecal material enters the appendix and is returned to the cecum by peristalsis. If the return is obstructed and the fluid absorbed, the mass becomes inspissated and a fecolith is formed. As a result of irritation by the mass and of low grade bacterial activity, there is increased secretion of mucus, and from this inorganic salts are deposited on the surface of the fecolith to produce a calculus. Repetitions of the cycle cause both a gradual increase in size and the grossly characteristically laminated appearance. Chemical analysis discloses the following composition: 25 per cent calcium phosphate and other inorganic salts, 20 per cent organic residue, and most of the rest soaps, koprosterol and cholesterol.

Worm Infestations.—Worm infestations of the appendix are quite common. Among others the following have been encountered, *enterobius vermicularis*, *trichocephalus trichiurus* ova, *strongyloides stercoralis* larvae, *necator americanus* ova, *hymenolepis nana* ova, *taenia* ova and *ascaris lumbricoides* ova. *Enterobius vermicularis* or pin worm is reported as occurring in from 1 to 32 per cent of all removed appendices in the United States. The higher figures are probably correct, because they are obtained by concentration methods rather than by gross or the usual microscopic examination of appendiceal content. While ordinarily exyuris infestation produces no lesion or symptoms the worm may occasionally penetrate

the wall and produce a focal infiltration of a foreign body type. At other times, an accumulation of the parasites may occlude the lumen and thereby, predispose to an ordinary acute appendicitis. In histologic sections, one not infrequently sees the worms in the wall of the appendix without a surrounding leukocytic or fibrotic reaction. These are interpreted as postmortem migrations.

Trauma—Trauma to the appendix is rare, but in industrial work, it looms as an important factor from the standpoint of compensation. It appears that the most common predisposing factor is adhesions that bind steadfastly one portion of the appendix to an immobile structure while the rest of the organ is free to shift about. Trauma in the form of a fall or blow occasions a tear which is followed by an acute inflammation. To minimize external violence as a cause of appendicitis, it has been stated that (1) there must not be a previous history of infection, (2) the injury must be severe enough and in the proper location and (3) the symptoms must follow the accident.

Fecal fistula—This usually occurs through the operative cutaneous wound, less commonly into the rectum and rarely into other organs such as the ileum. The following remarks pertain to *abdominal wall fistulas*. One-third of all such tracts follow operations on the appendix and in most of these cases there is, at the time of surgical interference, an abscess or peritonitis. Conversely, however, only about 3 per cent of all abscesses and peritonitis following appendicitis eventuates in fecal fistula. The causes of the abnormal communications may be listed as (1) failure to excise all devitalized tissue, (2) failure to remove the fecolith from the base of the appendix in cases where the abscess is drained and the vermiform process is not removed, (3) improper types and placement of drainage tubes, (4) reopening of the appendiceal stump (some say because it has been inverted and others say because it has not been inverted) and (5) injury of the bowel wall at the time of the second operation. The *internal opening* of the fistula is in the cecum in three-quarters of all cases, in the appendiceal stump and ileum in most of the rest, and rarely, in the sigmoid colon. The *diagnosis* is usually easy for fecal material extrudes on to the abdominal wall. When the tract, however, is less patent, it may be difficult to distinguish between a fistula and a colon bacillus infection. In such cases, roentgenograms following the injection of radio-opaque material into the abdominal ostium or a barium enema may be of value. Most appendiceal and cecal fistulas heal spontaneously. The remainder and most of the ileal communications are treated surgically. The ultimate *prognosis* is good.

Intussusception—This is uncommon. The cause is the same as it is in intussusception of the small intestine, that is, some pathologic state that, acting as a foreign body, is extruded by vigorous peristalsis. The primary conditions forming the apex of the intussusception have been listed as prolapse of the mucosa into the cecum about a fecolith, adenoma, nodule of active inflammation at the base, fibrous nodule in the same area, hyperplasia of lymphoid tissue, spasm of the muscle at the appendiceal-cecal junction, and

too large of an inverted appendical stump. The *anatomic* possibilities are (1) appendix into appendix, (2) appendix partly or wholly into the cecum, (3) appendix into cecum or ascending colon and then the cecum into the ascending colon or the colon into the colon until the apex reaches even the anus, and (4) inversion of the appendical stump. *Clinically*, intussusception of the appendix is usually found in young children to adolescence. Typically, there are attacks of colic that last one to three minutes and are followed by several hours of freedom, vomiting in some instances, passage of blood and mucus per rectum, loss of weight if the condition is chronic, and manifestations of obstruction if the colon is invaginated. A barium enema may show a filling defect. *Treatment* is operative and consists of reduction of the invagination and appendectomy. If the colon forms the intussusciens and reduction is impossible, then some form of resection is mandatory. The *prognosis* depends upon the degree of intussusception, the necessary operative procedure, and the age and condition of the patient.

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Chapter XIII

LARGE INTESTINE AND ANUS

LARGE INTESTINE

EMBRYOLOGY

THE development of the large bowel has been briefly considered in Chapter XI. As already noted, the portion of the dorsal mesentery opposite the small intestine becomes anchored to the posterior abdominal wall in an oblique direction. Its lateral flanges (which constitute the ascending and descending mesocolons), having elongated rapidly, carry the corresponding portions of the bowel laterally in the abdomen. As they become pressed against the posterior abdominal wall, they fuse with the peritoneum and these portions of the gut thus become steadfastly affixed. The mesenteries of the transverse and sigmoid colons remain free while that of the rectum obliterates.

ANATOMY

The large intestine is about 1.5 meters long. It differs from the small bowel in that it contains sacculations, appendages of serosal fat called appendices epiploicae, and a grouping of the external muscle into three bands known as taeniae. It is divided into the following *six portions*, (1) *Cecum* measuring 6 x 7.5 cm. This is the first part located in the right iliac fossa, resting upon the iliac muscle and covered by the omentum, sometimes coils of small intestine, and the abdominal wall. (2) *Ascending colon* measuring about 15 cm. in length. It ends in the hepatic flexure which abuts against the liver, and it covers the lower and lateral part of the right kidney. (3) *Transverse colon* which measures approximately 50 cm. in length and is limited by the hepatic and splenic flexures. It forms an arch whose concavity is directed up and back and, variable in position, it is located in the umbilical or the epigastric regions. Its posterior surface covers part of the duodenum and head of the pancreas; the upper surface contacts the liver, gall bladder, stomach and spleen, and the lower surface over-rides the small intestine. (4) *Descending colon* measuring about 25 cm. in length, located in the left hypochondriac and lumbar regions and covering the lower part of the left kidney. (5) *Sigmoid colon* forming a loop about 40 cm. long that starts at the brim of the pelvis and ends opposite the third sacral vertebra. It is mobile and contacts the rectum, bladder, uterus and adnexa as the case may be. (6) *Rectum* which measures 12 cm. in length and ends 2 to 3 cm. below the tip of the coccyx. It differs from the rest of the large bowel in that it has no sacculations and the external muscle coat forms a continuous layer rather than taeniae. The rectum rests on vessels and nerves and lies behind the bladder, seminal vesicles, ductus deferens and prostate or the

uterus and vagina. Its lumen is interrupted by the transverse semilunar folds (Houston's valves) projecting from the right and left sides and from the anterior surface respectively. The colon is supplied by the colic and sigmoid branches of the mesenteric arteries and the rectum by the superior hemorrhoidal branch of the inferior mesenteric artery. The innervation is from the sympathetic and parasympathetic nerves and the lymphatics drain into the mesenteric and pre-aortic nodes.

Histologically, the mucosa is smooth for it contains no folds or villi (Fig 297). The glands of Lieberkuhn are straight and regular, measuring to 0.7 mm in length. They are rich in goblet cells, contain a few argentaffine cells, but are, as a rule, devoid of Paneth cells. The lamina propria contains varied numbers of cosmophils and scattered solitary lymph follicles, the muscularis mucosa is well-



FIG 297 —Normal colon $\times 375$

developed, the submucosa is the same as in other portions of the intestinal tract and the external muscle coat as already stated is heaped into bundles called taeniae.

PATHOLOGY

Congenital Anomalies—Developmental malformations of the colon eventuate from abnormalities of growth, migration, fixation and recanalization. Accordingly, they may be enumerated as follows: microcolon, dolichocolon (redundancy), congenital megacolon, non-rotation, high cecum, low (pelvic) cecum, retroposition (transverse colon behind the stomach, duodenum, and small intestines), interposition (transverse colon between the diaphragm and the liver, stomach and spleen), hypermobility of any portion, absence of any part or all, stenosis, atresia, diverticula, duplications, triplications and cysts. Some of these lesions are of little

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lus, fecal impaction and perforation with peritonitis. The mortality rate reaches 50 per cent in the first three years of life but is considerably lower thereafter.

Diverticula of the large bowel may be congenital or acquired. The former are rare, usually single, most frequent in the cecum, have no predilection for either sex and occur at all ages. Acquired diverticula are found in about 5 per cent of all people over the age of forty years, are infrequent below the age of thirty years, and affect two males to every female. They usually involve the sigmoid and descending colons and are almost always multiple. (Hence the condition is known as diverticulosis.) The causes of acquired diverticula are unknown, but it is generally thought that there is a local area of weakness in the wall combined with increased intra-

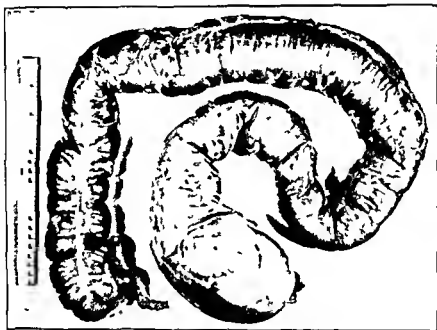


FIG. 208.—Congenital megacolon removed from a boy three years old.

luminal pressure. The weakness is said to be due to thinning of the muscle as a result of the formation of the hernie, to the entrance of the blood vessels, disturbance of sympathetic innervation, low grade infection, old age degeneration, and excess accumulation of fat in the appendices epiploicae. Increased intraluminal pressure is ascribed to the presence of gas and feces, both of which are consequent to constipation. Diverticula are asymptomatic. When they become inflamed the condition is called *diverticulitis* and is accompanied by abdominal pain, nausea, vomiting, tenderness, rigidity, leukocytosis and fever, and less frequently by flatulence, diarrhea alternating with constipation, rectal bleeding and a palpable mass. The localizing manifestations will be in the left or right lower quadrants of the abdomen depending upon the site of the lesions. In diverticulitis of the lower portion of the bowel, a sig-

clinical significance while others are extremely rare. The only two worthy of more detailed consideration are congenital megacolon and diverticula.

Congenital megacolon is also known as congenital idiopathic dilatation of the colon and Hirschsprung's disease. It is a progressive dilatation, elongation and hypertrophy of the large bowel and is ordinarily divided into (1) an *acquired* type which is secondary to some obstruction such as stenosis, spasm, inflammation, tumor and so forth and (2) an idiopathic or *congenital* type wherein there is no demonstrable etiological factor. The latter alone will be considered here. The *theories* regarding its cause may be listed as increase length of mesentery, redundancy, achalasia of the anorectal or rectosigmoid junctions, inflammation of Auerbach's plexus, overactivity of the lumbar sympathetics, hypoactivity of the sacral parasympathetics, and simply an imbalance of the autonomic nervous system. The disease is said to happen once in every 9000 people; it is noted from birth to senility with most of the cases occurring in infants and young children, and it affects four males to every female. The chief *symptom* is constipation which starts at birth. There may be only one bowel movement every three or four weeks and this is occasioned by putrefaction of the intestinal contents. As a result, the stools when present are often copious and offensive. The abdomen becomes greatly distended and there may be pain, vomiting, headache, stunting of growth, weakness, anorexia and failure to gain weight.

In almost all of the cases the sigmoid is involved, and the distention diminishes proximally affecting varying lengths of the bowel but frequently extending to the cecum (Fig. 298). At the other end the process usually stops abruptly at the recto-sigmoid junction, although at times it extends to the anus. The bowel is redundant, elongated, looped and dilated to as much as 35 cm. in diameter. The mesentery too is thickened and elongated and the wall of the colon is thick, grey, leathery and shows a disappearance of the taeniae and sacculations. The mucosa may be grossly intact or disclose stercoral ulcerations. *Histologically*, all coats are hypertrophied with a relative increase in thickness of the circular musculature. The mucosa frequently shows hyperplasia, focal necrosis and non-specific ulcers; the submucosa is thickened by fibrous tissue and reveals increased vascularity, neutrophils, lymphocytes and plasma cells. The ganglion cells and nerve fibers of Auerbach's plexus are smaller and fewer in number than normal and in addition the cells disclose vacuolization.

In fully developed cases, the *diagnosis* is easily made, while at the onset the disease must be differentiated from anal spasm, rectal stricture and dolichocolon. *Treatment* is always medical first and consists of enemas, laxatives, regulation of diet and administration of parasympathomimetic drugs such as mecholyl bromide, syntropan, prostigmin and physostigmine. If these fail surgery is indicated. It consists of colostomy, resection of the colon, sympathectomy in cases that respond to spinal anesthesia, and emergency procedures when complications arise. The latter consist of volvu-

mass (3) Obstruction which in the acute stage is due to edema and inflammation and in the chronic stage to fibrosis, adhesions and angulation of the bowel wall (4) fistulas extending to the urinary bladder, adjacent bowel, other viscera, and anterior abdominal wall (5) Pylephlebitis

A correct diagnosis of diverticulitis particularly of the cecum is extremely difficult to make. The condition is usually confused with acute appendicitis, perforated duodenal ulcer, acute cholecystitis, carcinoma and ileo-cecal tuberculosis. Treatment is prophylactic in the form of a low residue diet, bland laxatives like mineral oil and occasionally, drugs like belladonna. In uncomplicated diverticulitis, it consists of bed rest, heat to the abdomen, antispasmodics, nothing by mouth and fluids parenterally. This gives satisfactory results in from one-half to two-thirds of all cases. Surgical intervention is indicated in most of the aforementioned complications. It consists of drainage of abscesses, closure of perforations and relief of obstruction by colostomy, cecostomy or partial resection. The overall operative mortality is about 16 per cent. Recurrences of infection in medically treated and in surgically treated, but non-resected diverticula, are common.

Inflammation—Non-specific Inflammations—Three important surgical lesions of the large intestine that may be placed in this category are acute phlegmonous cecitis and colitis, ulcerative colitis and mucous colitis.

Acute Phlegmonous Cecitis and Colitis—This is analogous to a similar process in the stomach and small intestine both of which have been considered in the two preceding chapters. In the large bowel, the lesion is most common in the cecum, is confined to an oval or round sharply demarcated area of the gut or involves larger segments of the intestinal wall, and has the same gross and histologic appearance as it does in the upper portions of the gastro-intestinal tract. The chief manifestations are fever, pain, vomiting, obstruction and abdominal mass. The lesion is thus confused with appendicitis, carcinoma and tuberculosis. Treatment is surgical resection. The mortality is about 10 per cent.

Ulcerative Colitis—Through usage this term is reserved for ulcerating lesions of the large intestine of undetermined etiology. The disorder has also been called colitis gravis, thrombo-ulcerative colitis, idiopathic ulcerative colitis, cryptogenic ulcerative colitis, chronic suppurative colitis and non-specific ulcerative colitis. As in other obscure lesions so in this disease speculation regarding the causative agents has been rampant. The following are some of the factors that have been implicated (1) bacteria such as streptococcus, dysentery bacillus, and tubercle bacillus, (2) virus, (3) amoeba, (4) fungi, (5) serum and vaccine therapy, (6) allergy to food and bacteria, (7) dietary deficiencies, (8) metabolic disturbances reducing the resistance of the mucosa and (9) neurogenic influences acting by way of (a) psychogenic impulses resulting from apprehension, tension, worry and fear, (b) excess vascular spasm or dilatation, (c) excess mucosal secretion and (d) spasm of the muscles. Ulcerative colitis occurs in 9 of every 1000 people with gastrointestinal

moidoscopic examination may reveal the openings of the pouches, spasm, hypermotility, obstruction, sharp angulations, mucosal edema and an external mass. A barium enema may disclose serrated linear filling defects, spasm, hypermotility and obstruction.

In the *cecum*, the diverticula are located in the atero-lateral or the postero-medial borders, whereas in the *colon*, they are almost always between the mesocolic and antimesenteric taenial bands and rarely between the antimesenteric taeniae. They vary in size from a few millimeters to 4 cm. in greatest diameter and externally are frequently concealed by fat (Fig. 299). They are of a bluish color, round or flasked shaped, thin walled, and communicate with the lumen by wide or narrow, round, slit-like or pin point openings.



FIG. 299 — Diverticulosis of the colon showing several mucosal openings and seven serosal outpocketings. The fat which covered these has been dissected away.

If these are small the diverticula are usually filled with fecal material or fecoliths, but if they are widely patent their lumens are empty. *Histologically*, congenital diverticula disclose all the layers of the intestine whereas acquired diverticula are usually devoid of muscle. Inflammation, as a rule, results from obstruction of the pouches by fecal material. At first it is confined to the diverticulum but soon it spreads to the adjacent bowel wall and to the peri-intestinal tissues. Microscopically, it is entirely non-specific and consists of congestion, edema and local extravasation of leukocytes. In some cases, this is followed by resolution or by granulation tissue and residual fibrosis. In others, the inflammation progresses and may be accompanied by the following *complications*. (1) Acute perforation and generalized peritonitis. This is unusual for the infection is as a rule attended by a peri-diverticulitis which walls off the impending rupture. (2) Peridiverticular abscess. This is the most common complication and, as a rule, results in a tender pelvic

plete colectomy. Ulcerative colitis may pursue a rapid course terminating in death in a few months, or symptoms may be few and relapses several months or many years apart. The mortality is reported as varying from 10 to 30 per cent.

Mucous Colitis—Mucous colitis is part of a general autonomic nervous system instability characterized by undue irritability of the colon, spasm and excess secretion of mucus. It has also been called chronic colo-spasm, irritable colon, unstable colon, spastic colitis, mucomembranous colitis, dyssynergic colon, catarrhal colitis and toxic colitis. The disorder is truly functional and exhibits no specific or regular pathologic changes. In fact at autopsy, the colons from patients with the condition who have died of other causes are usually entirely normal. The predisposing etiological factor is a



FIG. 300—Chronic ulcerative colitis. The wall is thick and fibrotic and the mucosa is ulcerated and covered with pseudopolyps.

neuromuscular and neuroglandular abnormality, while the precipitating causes are (1) local irritants such as cathartics, colonic irrigations and sensitivity to foods and (2) mental disturbances in the form of nervous tension, anxiety, worry, introspection and unhappiness. The condition is usually found before the age of forty years and is more frequent in women. Local symptoms are variable and consist of abdominal pain or discomfort, constipation, diarrhea or constipation alternating with diarrhea. Mucus, usually present in small or large amounts is arranged loosely, in membranes or in coats. Sigmoidoscopic examination is normal and roentgenograms show spasticity. The diagnosis is made by taking a careful history, which is usually given in great detail, and by excluding organic lesions. Treatment is medical and includes reassurance, a bland diet, mineral oil and belladonna.

medical, while in the presence of obstruction, perforation, abscess or fistula, it is surgical.

Syphilis of the colon and rectum may be of the *hereditary* or *acquired* types, and is similar to that of the small intestine. Rarely, the rectum may be the site of a chancre. *Symptoms* may simulate those of ulcerative colitis (diarrhea, blood in the stools, weakness and loss of weight) or they may simulate carcinoma of the rectum (tenesmus and ribbon like stools). *Clinically*, the diagnosis is difficult to establish. Just because a patient has a positive serologic test for syphilis, it does not necessarily follow that a lesion in the bowel is syphilitic. It is stated, however, that a positive *diagnosis* is justified in the presence of a history of exposure, typical proctoscopic and sigmoidoscopic appearance of the lesions (see preceding chapter), a positive serologic test for syphilis, and response to anti-syphilitic therapy. It is confirmed by finding the spirochetes in the tissues and by the characteristic histologic picture.

Actinomycosis of the gastrointestinal tract involves the ileocecal region in 75 per cent of cases. The organisms are of the human strain and gain entrance by being swallowed. *Symptoms* are of two types. (1) Acute in which case they resemble acute appendicitis. The usual story is that this organ is removed and the wound heals. Shortly thereafter there are chills, fever, weakness and toxicity followed by an abscess which breaks down leaving a persistent sinus tract. (2) Chronic. In such cases the first manifestation may be a painless tumor mass in the right lower quadrant, or there may be associated pain and constipation. The lesion evolves and extends in the manner already described in the chapters on the skin and mouth. Ultimately, there is a hard brownish mass that involves the abdominal wall, breaks down and discharges one or many sinuses on to the surface. When the lesion is still confined to the peritoneal cavity, it is usually mistaken for tuberculosis or carcinoma, but the formation of sinus tracts should always arouse suspicion of actinomycosis. Examination of the discharges for the causative organism readily confirms the diagnosis. *Treatment* consists of administration of potassium iodide and antibiotics, of surgical excision and of roentgen therapy. *Complications* are (1) abscess formation—perinephric, subphrenic, rectal, psoas, pelvic, hip, groin and abdominal wall, (2) fistulas—to the exterior and abdominal organs such as urinary bladder and (3) widespread hematogenous dissemination. The *prognosis* is grave. Extensive lesions are seldom cured.

Tumors—Neoplasms of the large intestine closely parallel those of the small bowel. Since an outline of these has been presented in the preceding chapter, a reclassification here is not necessary. Despite the wide variety of possible tumors only a few occur with sufficient frequency to be of clinical significance. These consist of polyps, endometrosis, carcinoma and lymphoblastoma.

Polyps—This term is used here merely because it is universally accepted. As already stated, it should be further qualified for as it stands it merely means a pedunculated tumor of the mucosa. In connection with the large intestine, however, it has become synonymous with an epithelial growth and includes both papilloma and aden-

Polyps or polyposis should be suspected in a patient with an insidious on-set of diarrhea and mucus and blood in the stools. The diagnosis is confirmed by digital, proctoscopic, sigmoidoscopic and roentgenographic examinations. The latter includes a barium enema with post-evacuation and post-irrigation films in which



FIG. 302 — Pedunculated adenomatous polyp of the colon



FIG. 303 — Polyposis of the colon

polyps are visualized as filling defects. Biopsy or histologic examination of an entire polyp is always necessary to rule out cancer. Treatment is surgical. If the lesions are few and low down, they are moved or destroyed proctoscopically, if they are more proximal, treatment is colotomy and excision, while if they are more numerous,

oma. A single lesion is called a *polyp*, several are called *polyps*, and numerous growths are known as *polyposis*. Polyps may be divided into two *classes*; (1) *acquired* which arise on an inflammatory basis, are not truly new growths and are referred to as pseudopolyps and (2) true or *congenital*. These are again subdivided into single and multiple (polyposis). The latter are familial in most instances and are, therefore, hereditary. The disease is transmitted by both sexes. If the genes are dominant the disorder will occur in every generation, but if they are recessive then both parents must possess them before the condition appears. The incidence of polyps at postmortem is recorded as varying from 2.37 to 69 per cent of all cadavers. Males are affected twice as frequently as females and although the extreme recorded ages are two and eighty years, the tumors are rare before the age of thirty years, and the greatest incidence is between the sixth and eighth decades. Single and small lesions rarely produce *symptoms*. When they become malignant there are alteration in the stool, change in bowel habits and passage of blood and mucus by rectum. In polyposis there are abdominal cramps, mucus and blood in the stools, diarrhea, loss of weight, nausea, loss of appetite, fatigue and vomiting.

While polyps occur anywhere in the large bowel the favored *sites* are the sigmoid and rectum. As already stated the numbers vary from one to hundreds and they range in size from 1 mm. to 9 cm. with usual measurements of 1 mm. to 2 cm. (Fig. 302 and 303). At first, most of the growths are sessile but later, as a result of peristalsis they become elongated and pedunculated. The surface is regular, finely granular or deeply serrated and of a grey or greyish-brown color. The tumor is moderately firm but not hard and is freely movable at the base. A malignant change is said to occur

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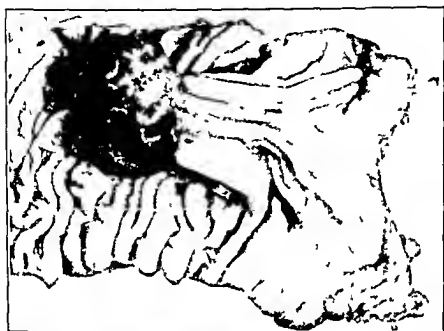


FIG. 302—Pedunculated adenomatous polyp of the colon

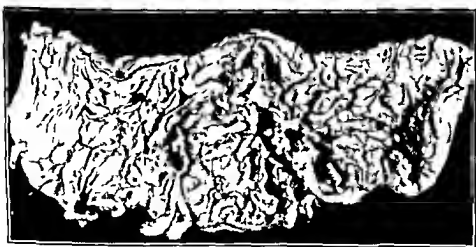


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it consists of partial or complete colectomy. The *prognosis* is good if therapy is instituted early.

Endometriosis. This is considered in more detail in the chapter on the female genital tract. It is mentioned here because next to the adnexa and uterus, the bowel is the most frequent site of the disease. The majority of lesions occur in the rectum and sigmoid. The disorder affects women between the ages of thirty years and the menopause. *Symptoms* are more severe just before or at the onset of menses and consist of (1) pain in the lower abdomen, rectum and down the thighs which is aggravated by defecation, (2) constipation or diarrhea and (3) nausea and vomiting. Rectal examination may

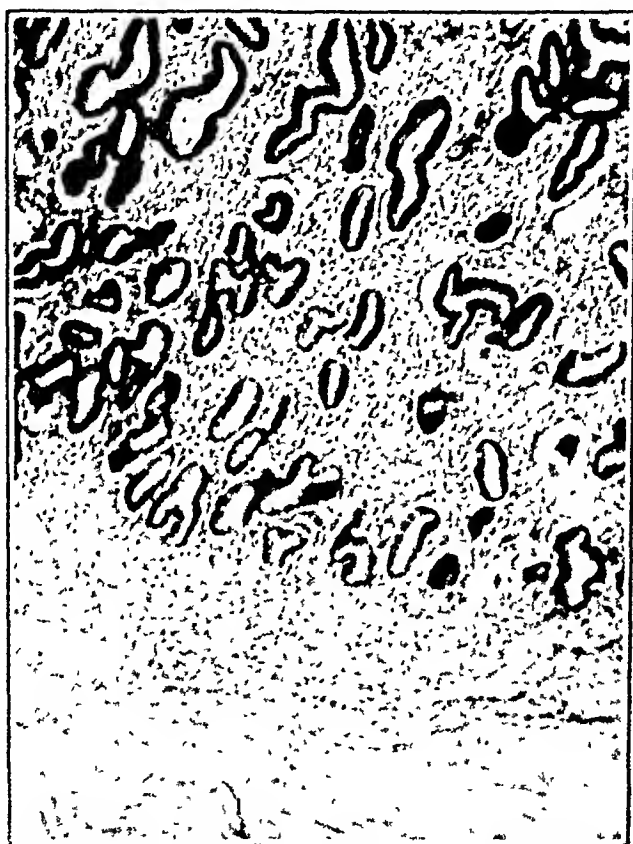


Fig. 234. Endometriosis on the colon. The papillae confined to the crypts.

be necessary when obstruction is marked and fibrosis severe. The prognosis is good.

Carcinoma—Carcinoma of the large intestine is said to constitute 8 per cent of all cancers and to cause 1 death yearly for every 10,000 people. The usual age period varies from forty to seventy years with an average of fifty-seven years. In the colon, the incidence in males equals that in females, whereas in the rectum, it is twice as common in men as it is in women. The duration of symptoms varies on an average from six to ten months. They consist of any combination of the following: gross or occult blood in the stools, alteration of bowel habit (frequent stools, diarrhea or constipation), alteration in the form of the stool, abdominal pain or cramps, rectal pain, tenesmus, loss of weight and weakness. The only physical



FIG. 305.—Ulcerating carcinoma of the rectum.

findings may be a palpable mass, either through the abdominal wall or digitally in the rectum, and anemia. Proctoscopic and sigmoidoscopic examinations are of aid in detecting tumors in the distal portion of the bowel, and roentgenograms with the aid of barium disclose obstructive lesions and filling defects.

The distribution of carcinoma of the large intestine varies considerably according to different writers. The approximate order of frequency is rectum 50 per cent, sigmoid 22 per cent, descending colon 6 per cent, transverse colon 5 per cent, ascending colon 5 per cent, cecum 5 per cent, and the flexures, ileo-cecal valve and anus 7 per cent. The tumors start either in the crypts of Lieberkuhn or in 14 to 34 per cent of cases in pre-existing polyps (adenomas and papillomas). Growth is particularly slow in the rectum where it is stated that it takes six months for the lesion to reach one-quarter

of the distance around the lumen and eighteen months for it to penetrate to the serosa. *Grossly*, as in other portions of the gastrointestinal tract, the neoplasm may take on one of three appearances—ulcerative, polypoid, or infiltrative. *Ulcerating* lesions are perhaps the most common (Fig. 305). They exist as round or oval masses that are often distributed transversely in the wall, that occupy varying portions of the circumference and that usually measure 3 to 6 cm. proximo-distally. These tumors ulcerate as they penetrate. The edges are thus only slightly raised, moderately firm and ill-defined. The centers are superficially ulcerated or deeply excavated. Their floors are covered with grey necrotic friable tissue and their bases are formed by muscle or serosa which

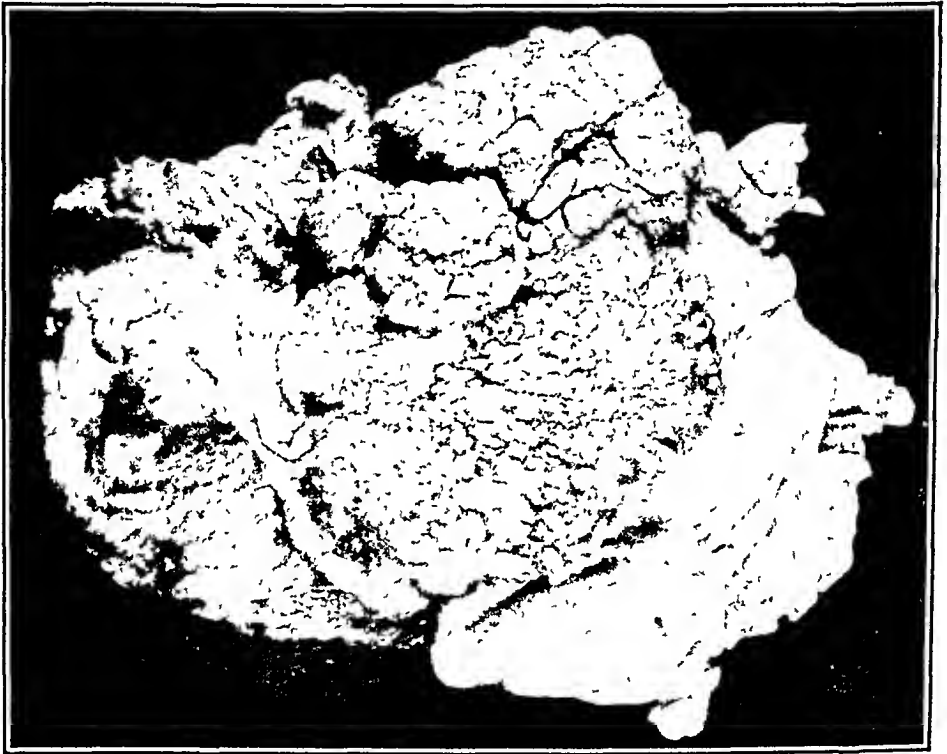


FIG 306 —Polypoid carcinoma of the colon.

is infiltrated with the neoplasm. It is this type of tumor that may erode a vessel to produce massive or fatal hemorrhage, that may perforate to produce peritonitis, or that may become adherent to another viscus to produce a fistula. The second most common type of tumor is the *polypoid* variety (Fig. 306). This starts as a carcinoma or represents a malignant transformation of a polyp (adenoma or papilloma). The neoplasm grows into the lumen to produce a fungating, moderately firm but friable, pinkish-grey cauliflower-like mass that usually measures to as much as 6 cm. in diameter. The surface may be intact or superficially ulcerated and the base penetrates the wall for varying depths. The *infiltrative* type of growth is the least common (Fig. 307). Unlike in the stomach, this variety of tumor in the large bowel penetrates the tunics and, simultaneously, encircles the lumen relatively early

but it does not extend over great distances proximo-distally. The result is a constricting, hard, nodule-like tumor that reduces the lumen to a diameter of a few millimeters and that seldom measures more than 3 cm in length. Its mucosal surface is only superficially ulcerated. *Histologically*, as in other portions of the gastrointestinal tract (see Chapter X), the growths vary from a well-differentiated adenomatous structure that is difficult to differentiate from an adenoma to a completely undifferentiated structure that resembles a sarcoma. The signet ring or the colloid type are also found but with much less frequency than in the stomach.

Carcinoma of the large bowel spreads (1) by local extension to involve first the wall of the gut and then any other tissues or organs that may touch it, (2) by lymphatics usually in a cephalic manner

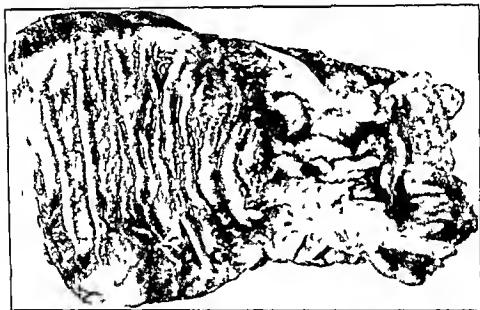


FIG. 307.—Infiltrating carcinoma of the colon.

and rarely in a caudal direction. Regional lymph nodes at the time of operation are involved in from 36 to 68 per cent, (3) by veins first to the liver and then to the lungs and any other organ or tissue. The incidence of tumor emboli in resected specimens are reported in from 16.6 to 90 per cent and it is said that visceral metastases develop in over nine-tenths of such cases and (4) by the peri-neural spaces. This form of spread is reported as occurring in 30 per cent of resected specimens. It is probably responsible for pain which occurs in 90 per cent of the cases and it is responsible for local recurrences in 80 per cent of the cases.

The *diagnosis* of carcinoma of the large gut is made from a consideration of the history, a palpable intra-abdominal mass, digital rectal examination, proctoscopic and sigmoidoscopic examinations and barium enema. The only effective *treatment* is complete surgical excision. At the present time, resectability is recorded

or severe cases of various surgical procedures. Some of these consist of cauterizing or excising the excess mucosa, narrowing the anus, strengthening the natural supports of the rectum and resection.

Foreign Bodies—These gain entrance into the large intestine by being *swallowed* or inserted from below. The former are not common, they usually lodge in the cecum, and they are sometimes arrested by obstructive lesions of the bowel. Those inserted from below are more numerous and usually lodge in the rectum. They occur in pervers, insane or as a result of accidents. Some of the objects recorded are tumblers, nails, pins, stones, fruit, bottles, whiskey glasses, mortar pestle, ox horn, electric light bulb, chicken bones, glass tubing, broom handle, pig's tail and tool box containing gun barrel, hack saws, syringe, file, coins, thread and tallow. Foreign bodies may cause trauma with bleeding, perforation and constipation. Most of the rectal ones can be removed with the aid of a proctoscope and anesthesia. The prognosis depends upon the damage done and the duration of the sojourn.

Obstruction—Obstruction of the large intestine may be caused by the following, (1) *congenital* lesions as absence of a segment, atresia, stenosis and fecal impaction in megacolon, (2) *inflammatory* processes as acute phlegmonous cecitis and colitis, diverticulitis, ulcerative colitis, regional colitis, tuberculosis, syphilis, actinomycosis and botryomycosis, (3) *tumors* both intrinsic and extrinsic and (4) *mechanical* factors such as volvulus, foreign bodies, intussusception and prolapse of the rectum.

Fecal Fistula—This is not common. Over one-third of all cases occur in the right lower quadrant as a result of appendicitis or its complications. The rest are found in other portions of the intestinal tract. They may be divided into (1) *internal fistulas* occurring between portions of the intestinal tract or between the intestinal tract and some other organ, e.g., gastrocolic, rectovaginal and rectovesical and (2) *external* occurring between the intestine and the outside. The causes of fecal fistulas may be listed as (1) *congenital*—patent omphalo-mesenteric duct, rectovesical, rectourethral or rectovaginal, (2) *inflammations*—abscess (prostatic, peri-rectal, etc.), diverticulitis, regional ileitis and colitis, tuberculosis, and actinomycosis, (3) *malignant tumors*—carcinoma of the bowel, prostate and ovary, and (4) *mechanical factors*—surgical as colostomy, etc., strangulated hernia, gunshot or other wounds, instrumentation such as cystoscopic (rectovesical), and irradiation as for carcinoma of the cervix (rectovaginal). The diagnosis of external fecal fistula is usually easy but when the tract is small it may be confused with B. coli infection. In such cases, roentgenograms following the injection of the ostium with radio-opaque material will often outline its course and disclose its true nature. A similar procedure is usually resorted to in cases of internal fistulas. In the absence of granulomatous disease as tuberculosis or actinomycosis and in the absence of a malignant tumor, most fistulas close spontaneously. A few, however, persist and the causes of these have been listed as the presence of mucosal lining, rigid fibrous walls, herniation in abdominal wall, peristaltic traction, foreign bodies

as 90 per cent of all cases, the hospital mortality as about 20 per cent, the operative mortality in resectable cases as 4 to 10 per cent and the five year survival rate as about 15 per cent. In irresectable cases, roentgen and radium therapy is accompanied by a 5 per cent five year survival. The *causes of death* postoperatively are peritonitis, abscess and pulmonary disorders. In untreated cases, the mean duration of life from the onset of symptoms is fourteen months.

Lymphoblastoma. Here as elsewhere the term lymphoblastoma includes any primary tumor of lymphoid tissue principle among which are lymphosarcoma, Hodgkin's disease and reticulum cell sarcoma. The age distribution, namely fourth and fifth decades, is the same as in the small intestine but in the large bowel the recorded cases have been almost exclusively in males. *Symptoms* consist of abdominal pain, constipation, diarrhea, intra-abdominal mass, rectal bleeding, and pruritus ani. The disease may be part of a generalized disorder, but there are cases in which the bowel tumors are the primary and only lesions. The *growths* start in the solitary lymph follicles of the submucosa and they produce (1) *diffuse* infiltrations of the wall with grey moderately firm tissue in which case the normal tissues are accentuated or (2) they result in *polypoid* masses that project into the lumen. Sometimes in rectal lymphoblastoma, the tumor starts in peri-rectal lymph nodes and affects the bowel wall by direct extension. The *sites* of predilection are the rectum and the cecum. *Treatment* of lesions primary in the bowel is surgical excision followed by irradiation. The *prognosis* is generally not good, although a few five to fifteen year cures are recorded.

Mechanical Disturbances.—**Volvulus** in about one-third of all cases occurs in the large bowel. The favored sites are the cecum and ascending colon in cases of mobile cecum, and the sigmoid colon. *Rupture* of the large bowel has been considered in conjunction with the small intestine.

Intussusception.—In the large intestine this is uncommon. The more frequent sites are the cecum and ascending colon, the sigmoid and the rectum. The latter is known as *prolapse*. It consists of a protrusion through the anus of the mucosa or the entire thickness of the rectal wall. Mucosal prolapse occurs in early childhood and old age, whereas the entire wall protrudes at any time during adult life. The *causes in childhood* are listed as weak fixation of the rectum, high position of the bladder and uterus, absence of the sacral curvature, and straining due to diarrhea, constipation, and pertussis. In *adults* the causes are atrophy of the sphincter, injury to the sphincter at operation or parturition, weakness of the levator ani muscle, hemorrhoids, polyps and straining in enlargement of the prostate, urethral stricture, and at stools. The *manifestations* are a projection of the mucosa or a sausage-shaped mass through the anus. The latter is seen when the entire wall prolapses and is accompanied by obstipation. The protruded portion becomes infected, ulcerated and sometimes gangrenous. *Treatment* consists of eradicating the cause, regulating bowel movements and in persistent

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The mortality in type 1 is about 10 per cent, in type 2 about 15 per cent, in type 3 about 25 per cent and in type 4 about 60 per cent.

Anal Ducts—In about 50 per cent of anal canals there are vestigial glands or ducts that rise in the crypts of particularly the posterior portion and sinuously course inwardly and caudally to penetrate in some cases the internal anal sphincter. Most of them are lined by transitional epithelium in which there are also found mucous cells. These structures although appearing insignificant may be important in the development of fistulas, sinuses, abscesses and even carcinoma.

Inflammation—Non-specific Inflammations—These are two important lesions of the anus in this category—fissure and fistula.

Fissure of the anus is a tear or ulcer at the mucocutaneous line. It constitutes about 10 per cent of all anorectal diseases. Its cause is trauma in the form of hard stools, childbirth, straining, enema tips or foreign bodies. Its location in the majority of cases is in the posterior commissure—opposite the bifurcation of the sphincter. Examination discloses spasm of the anus and in the acute stages a non-specific ulcer. When it becomes chronic the base is composed of fibrous tissue, the edges are firm, and the adjoining skin proliferates and becomes edematous to form what is known as the "sentinel pile." A similar process in the upper border produces *papillae*. Symptoms consist of pain (due to spasm of the anus) which is aggravated by defecation. Fresh blood is frequently seen after a bowel movement. The most satisfactory treatment is excision of all the diseased tissue.

Fistulas of the anus are abnormal sinus tracts that have at least one opening in the mucosa and another in the skin, adjacent viscus or the intestinal mucosa at a different level. Tuberculosis is responsible for about 8 per cent of the fistulas. The rest are caused by ordinary pyogenic organisms. The disorder starts as an infection in the anal crypts and glands, whence it burrows through the sphincter muscles into the ischioanal fossa there forming an abscess. Due to inadequate drainage consequent to anal spasm, the mass enlarges and ultimately breaks through the skin, into the rectum, or into another pelvic viscus. The fistula is thus complete. Treatment consists of chemo- and antibiotic therapy, incision of the abscess and excision of the entire tract.

Specific Inflammations—Granulomatous lesions that will be considered under this heading are tuberculosis, syphilis, gonorrhea, chancroid, lymphopathia venereum and granuloma inguinale.

Tuberculosis of the anus is usually secondary to lesions elsewhere but occasionally, it is primary. It affects males three times as frequently as females, and it occurs in young adults. Symptoms consist of burning, itching, some pain and a disturbing discharge. The lesion occurs at the anal margin first as an elevation which soon breaks down to produce a round or oval, shallow ulcer. The edges are sharply defined, irregular and undermined, the floor is covered with a thick sometimes bloody discharge, and the base and edges are indurated. The histologic structure as in other areas is specific, but it may be necessary to examine several pieces of tissue before

(talcum powder, lycopodium, cotton and petrolatum), and a defect in the intestine too large for spontaneous closure. In such cases, some form of surgical excision of the tract and obliteration of the openings is necessary.

ANUS

EMBRYOLOGY

Early in embryonic life the cloaca forms a terminal cavity that is common to the intestinal and urogenital tracts. It is narrow and has a cloacal membrane closing its caudal surface and two ridges on its lateral wall. By the fifth week, a coalescence of these ridges and the downward growth of the urorectal septum separates the genitourinary tract from the intestinal tract. As the partitioning is being completed the narrow space is called the cloacal duct. At the seventh week, the cloacal membrane is divided into the urogenital membrane anteriorly and the anal membrane posteriorly. An inpocketing of the latter forms the proctodeum which increases in depth until the eighth week when it reaches the rectal bulge.

PATHOLOGY

Congenital Anomalies.—These may be divided into two, namely, (1) those associated with the formation of the anus and rectum and (2) the presence of anal ducts.

Abnormalities of the ano-rectal junction occur once in every 5000 births. They are ordinarily divided into *four groups*. (1) Incomplete rupture of the anal membrane or stenosis of the anus anywhere from 1 to 4 cm. above the external opening, occurring in from 25 to 33.3 per cent of all cases. (2) Imperforate anus when the obstruction is due only to persistence of the membrane, seen in comparatively few cases. (3) Imperforate anus with rectal pouch separated from the anal membrane and ending blindly. This is the most common abnormality being encountered in almost two-thirds of all cases. It is also the one in which fistulas between the rectum and bladder, urethra, vagina and perineum occur most frequently. (4) Normal anus and anal pouch with rectal pouch ending blindly. The two may be separated by a membrane or by a wide interval with only a connecting cord. These anorectal anomalies affect males four times as often as females. All except the first type are accompanied by *intestinal obstruction* and are, therefore, recognized within a few hours or at the most a few days after birth. It is also noted that there is no anal opening, no meconium on the diaper, or meconium coming from an abnormal opening. Roentgenograms with the infant inverted and an opaque object on the perineum will show the relation of the rectum (demonstrated by an air bubble) to the anus. *Treatment* in type 1 is dilatation, in type 2 cruciate incision of anal membrane and dilatation, in type 3 relieving the obstruction by colostomy, reconstructing the anorectal canal and repairing the fistulas, and in type 4 colostomy followed by perineal rectal repair.

ficial painless vesicle, papule or shallow erythematous ulcer. Ten days to six weeks later small *nodules* appear along the draining lymphatic vessels or in the nodes and are known as bubos. In males, the inguinal nodes are most frequently affected whereas in females, the ano-rectal nodes are involved. They become lobulated, matted, enlarged, firm and then break down and become soft. The skin becomes indurated, violaceous and ulcerates leaving discharging sinuses. The process spreads by burrowing everywhere leaving abscesses, sinuses and destruction and ultimately, involving the genitals, entire perineum, anus and rectum. The cutaneous destruc-



FIG. 308.—Granuloma inguinale affecting the entire anogenital region (Courtesy of Dr. Lewis C. Scheffey.)

tion and edema result in large polypoid sometimes pedunculated masses (elephantiasis) with intervening areas of scarring, wrinkling and dimpling. Anorectal lesions are primary in the mucosa or perirectally where they produce a circular stricture about 6 cm. from the external opening. *Histologically*, there are focal perivascular or in lymph nodes cortical proliferations of mononuclear cells. At their periphery, there are plasma cells, lymphocytes and sparse epithelioid and giant cells. Obliteration of the vascular lumens by pressure and coalescence of the granulomas results in the formation of focal central abscesses. When this occurs some of the peripheral monocytes are seen to contain intracytoplasmic inclusions the "Gambli bodies" (phagocytosed debris).

it is encountered. The organisms are demonstrable in cultures and in inoculated guinea pigs. *Treatment* consists of general anti-tuberculosis measures and local excision.

Syphilis of the anus and rectum may be *congenital* or acquired. The former is found in newborn infants as a peri-anal dermatitis with fragile skin and shallow fissures. *Acquired* syphilis occurs in any of the three stages. A *chancre* is rarely found at the anus. It is usually seen in females, but it also occurs in males as a result of sodomy. It is an irregular but sharp pink ulcer covered with thin serous discharge and disclosing no induration. Secondary infection changes these characteristics to a non-specific ulcer. Because of the associated moisture, there is maceration and fissuring. The sore is painful only when it is located within the anal canal. A diagnosis is made by dark-field demonstration of spirochetes. *Secondary* manifestations of syphilis consist of fissures, ulcers, papules and larger wart-like elevations known as *condyloma latum*. These are found at the anal margin or in the surrounding skin. Mucous patches, papules and plaques have been reported in the rectum but they are extremely rare. *Tertiary* lesions are uncommon and bizarre. Syphilitic stricture is rare but gummas are more common. They are more frequent about the rectum than the anus and present the usual sharply defined firm elastic mass that, as a rule, does not suppurate but that upon incision, yields a bloody serous discharge.

Gonorrhea of the anus and rectum is probably more frequent than generally supposed. It is more common in females with gonorrheal vaginitis, but it is also seen in males as a result of sodomy. Except for some burning and itching the disease is asymptomatic. *Examination* discloses hyperemia of the lower 6 to 7 cm. of the rectal mucosa and an excess of mucus. Ulceration followed by stricture may occur when the mucosa is traumatized, and fistulas and abscess occasionally arise consequent to infection of the anal crypts and glands. The *diagnosis* is established by identifying the organisms in smears. The disease is ordinarily self limited.

Chancroid or soft chancre is *caused* by the Ducrey bacillus—a small, non-motile, gram negative coccobacillus that is difficult to culture but that can be identified in smears. The sores are found in either sex as painful irregular peri-anal or anal fissures or ulcers. They bleed easily and spread rapidly by contact and by undermining the adjacent tissue. The *histologic* changes are not specific. *Treatment* consists of tartar emetic, specific serum and vaccine.

Lymphopathia venereum is known by many *other names* some of which are lymphogranuloma inguinale, paradenitis, strumous bubo, climatic bubo and, in women, esthiomene. It is a contagious venereal disease *caused* by a specific virus and transmitted by sexual contact. It prevails during the active sexual life, affects males as frequently as females, is found in all races but predominates in the colored and is most frequent among the lower classes.

A *primary sore* usually appears on the corona or the posterior vaginal wall but sometimes on other mucous membranes five to twenty days after exposure. It is evanescent and exists as a super-

ficial painless vesicle, papule or shallow erythematous ulcer. Ten days to six weeks later small *nodules* appear along the draining lymphatic vessels or in the nodes and are known as bubos. In males, the inguinal nodes are most frequently affected whereas in females, the ano-rectal nodes are involved. They become lobulated, matted, enlarged, firm and then break down and become soft. The skin becomes adherent, violaceous and ulcerates leaving discharging sinuses. The process spreads by burrowing everywhere leaving abscesses, sinuses and destruction and ultimately, involving the genitals, entire perineum, anus and rectum. The cutaneous destruc-



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Clinically, the primary sore is usually unnoticed. Following the initial lesions there are fever, chills, sweats, joint pains and leukocytosis. Secondary sores are sensitive, tender, bleed easily and discharge an abundant amount of seropurulent material. When the rectum is involved there are pain on defecation, constipation and obstipation. The *diagnosis* is made from the appearance of the lesions, intracutaneous inoculation of antigen (Frei test), complement fixation reaction and biopsy. *Treatment* consists of sulfonamides, vaccine, convalescent serum, dilatation of strictures and surgical excision of polypoid masses. Once the lesion is advanced the *prognosis* is poor.

Granuloma inguinale is also known as granuloma inguinale tropicum, ulcerating granuloma of the pudenda, pudendal ulcer and granuloma venereum. Although the mode of transmission is not definitely known, the lesion does occur on the genitals, perineum and in the anal (not rectum) canal. The *primary lesion* is a moist papule that rapidly ulcerates and spreads to repeat the process. Ultimately, there are large irregular ulcers with indurated sharp margins and covered with a fetid glary discharge (Fig. 308). Between these there are proliferations of epithelium and granulation tissue to produce condylomatous masses. There may be stricture of the *anal* canal, but inguinal lymph node involvement is slight and due to secondary infection. *Histologically*, the pathognomonic cell is a large monocyte that contains one or more intracytoplasmic cysts filled with small round or rod-like structures called Donovan bodies (stained best by Delafield's hematoxylin method or Giemsa's stain). The remainder is composed of granulation tissue heavily infiltrated with plasma cells and sprinkled with neutrophils. Lymphocytes are sparse or absent. *Treatment* consists of intravenous administration of tartar emetic which is specific for the disease.

Tumors.—The anus is composed of ectoderm and theoretically is, therefore, subject to any of the tumors discussed in Chapter I. Practically, however, the following lesions have been recorded most frequently: from the epidermis, a papilloma, Bowen's disease and carcinoma; from sweat glands, a hydradenoma; from fat, a lipoma; from connective tissue, a myxoma, fibroma and fibrosarcoma; from muscle, a myoma and myosarcoma; from pigment producing cells (probably of nervous origin), a melanoblastoma, and from lymphoid tissue, a lymphosarcoma. In addition, the following extra-anal neoplasms may present themselves at the anus: chordoma, teratoma, dermoid and adenomyoma from the recto-vaginal septum. Only two of the aforementioned tumors merit further consideration—carcinoma and melanoblastoma.

Carcinoma.—Carcinoma of the anus is usually of the squamous cell variety and constitutes from 1.7 to 5.7 per cent of all malignant tumors of the anus and rectum. Although its *cause* is not known the following pathologic lesions are said to be predisposing factors: leukoplakia, trauma, fistula, fissures, condylomas, hemorrhoids, and irradiation scars. The disease is more common in women than in men in the proportion of 3 to 1 and its peak incidence is the sixth decade. The earliest and most common *symptom* is persistent

bloody discharge. Other manifestations are late and consist of pain, tenesmus, diarrhea or constipation, itching, irritation and change in character of the stools. *Grossly*, the lesion simulates any of the many benign conditions in this area in 19 per cent of cases. The rest appear as nodular, flat or elevated ulcerating masses with firm hard grey bases and elevated undercut edges. In size they vary from a few millimeters to 10 cm in diameter and their location is in the perianal skin, the anal margin or the muco-cutaneous junction. *Histologically*, as already stated, most of the growths are of the squamous cell variety but occasionally, they are of the adenomatous and basal cell type. *Spread* is by local extension to the rectum, sphincters, perianal tissue, rectovaginal septum and prostate. Blood stream metastases are rare but lymphatic dissemination in all directions is common. Inguinal, mesocolic, iliac and periaortic nodes are most frequently affected. *Treatment* is wide surgical excision with dissection of the draining lymph nodes or irradiation. The *prognosis* is poor.

Melanoblastoma—Melanoblastoma of the anorectal region is rare. It arises from melanoblasts of the anal canal, whence it frequently invades the rectum. The tumor is usually single, sessile or pedunculated, light brown to black and varies in size from a few millimeters to 8 to 10 cm in diameter. *Histologically*, it does not differ from other melanoblastomas. Bleeding, pain and constipation are the most common symptoms. *Treatment* is wide excision. The *prognosis* is poor for the lesion recurs locally and metastasizes, among other places, to the liver and lungs.

Mechanical Disturbances—Aside from mucosal tears and direct trauma, two disorders that may be put in this category are hemorrhoids and bleeding.

Hemorrhoids—These are varicosities of the hemorrhoidal plexus of veins. The causes may be divided into predisposing and exciting. Predisposing factors consist of an inherited structural weakness, erect posture, absence of valves in the superior hemorrhoidal veins, lack of support by the surrounding loose areolar tissue, muscle strain and sedentary occupation. Exciting causes are those which reduce venous blood flow and consist of constipation, pregnancy, pressure of uterine, ovarian or prostatic tumors, circulatory impediment through the liver and anal cryptitis. Hemorrhoids are ordinarily divided into (1) *external*—these occur below the anorectal line and are dilatations of the external or the inferior hemorrhoidal plexus. Since they are covered with skin they are also called varicose, thrombotic or cutaneous anal tags and (2) *internal*—these occur above the anorectal line and are dilatations of the internal or superior hemorrhoidal plexus. They are usually the more troublesome, and appear as globular red to blue dilatations with smooth glistening surfaces and sessile or pedunculated bases. Their positions in the right and left posterior and right anterior quadrants are quite constant. Because of their location hemorrhoids are subject to trauma, ulceration, infection, thrombosis, necrosis and gangrene. They prevail between the ages of twenty and fifty years, and they affect males twice as frequently as females. *Symptoms* consist of

Clinically, the primary sore is usually unnoticed. Following the initial lesions there are fever, chills, sweats, joint pains and leukocytosis. Secondary sores are sensitive, tender, bleed easily and discharge an abundant amount of seropurulent material. When the rectum is involved there are pain on defecation, constipation and obstipation. The *diagnosis* is made from the appearance of the lesions, intracutaneous inoculation of antigen (Frei test), complement fixation reaction and biopsy. *Treatment* consists of sulfonamides, vaccine, convalescent serum, dilatation of strictures and surgical excision of polypoid masses. Once the lesion is advanced the *prognosis* is poor.

Granuloma inguinale is *also known* as granuloma inguinale tropicum, ulcerating granuloma of the pudenda, pudendal ulcer and granuloma venereum. Although the mode of transmission is not definitely known, the lesion does occur on the genitals, perineum and in the anal (not rectum) canal. The *primary lesion* is a moist papule that rapidly ulcerates and spreads to repeat the process. Ultimately, there are large irregular ulcers with indurated sharp margins and covered with a fetid glary discharge (Fig. 308). Between these there are proliferations of epithelium and granulation tissue to produce condylomatous masses. There may be stricture of the *anal* canal, but inguinal lymph node involvement is slight and due to secondary infection. *Histologically*, the pathognomonic cell is a large monocyte that contains one or more intracytoplasmic cysts filled with small round or rod-like structures called Donovan bodies (stained best by Delafield's hematoxylin method or Giemsa's stain). The remainder is composed of granulation tissue heavily infiltrated with plasma cells and sprinkled with neutrophils. Lymphocytes are sparse or absent. *Treatment* consists of intravenous administration of tartar emetic which is specific for the disease.

Tumors.—The anus is composed of ectoderm and theoretically is, therefore, subject to any of the tumors discussed in Chapter I. Practically, however, the following lesions have been recorded most frequently: from the epidermis, a papilloma, Bowen's disease and carcinoma; from sweat glands, a hydradenoma; from fat, a lipoma; from connective tissue, a myxoma, fibroma and fibrosarcoma; from muscle, a myoma and myosarcoma; from pigment producing cells (probably of nervous origin), a melanoblastoma, and from lymphoid tissue, a lymphosarcoma. In addition, the following extra-anal neoplasms may present themselves at the anus: chordoma, teratoma, dermoid and adenomyoma from the recto-vaginal septum. Only two of the aforementioned tumors merit further consideration—carcinoma and melanoblastoma.

Carcinoma.—Carcinoma of the anus is usually of the squamous cell variety and constitutes from 1.7 to 5.7 per cent of all malignant tumors of the anus and rectum. Although its *cause* is not known the following pathologic lesions are said to be predisposing factors: leukoplakia, trauma, fistula, fissures, condylomas, hemorrhoids, and irradiation scars. The disease is more common in women than in men in the proportion of 3 to 1 and its peak incidence is the sixth decade. The earliest and most common *symptom* is a persistent

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bleeding, protrusion, itching, leakage, constipation and, when complications arise, of severe pain. *Treatment* consists of surgical excision or of injection with a sclerosing fluid. The *prognosis* is good.

Bleeding.—Bleeding from the anal canal is a common symptom. If the blood is recognizable grossly, one speaks of *melen*a but if microscopic or chemical methods are necessary for its detection, one speaks of *occult blood*. In general, if the blood is bright red and on the outside of the stool, its point of origin is low in the intestinal tract such as the anus or rectum. If it is thoroughly mixed with the stool, it arises more proximally. A brown or black color indicates digestion and, therefore, the stomach or the upper portion of the small intestine as the point of origin. The two most common *causes* of bleeding from the anus are hemorrhoids and carcinoma of the distal end of the large bowel. Other causes may be listed as follows: (1) from the stomach—any of the lesions causing hematemesis which have already been enumerated in Chapter X, (2) from the small intestine—diverticula, Meckel's diverticulum, phlegmonous enteritis, duodenal ulcer, syphilis, regional enteritis, intussusception, and benign and malignant tumors, (3) from the large intestine—diverticulitis, ulcerative colitis, tuberculosis, polyposis, lymphoblastoma, foreign bodies, penetrating wounds and fissure and (4) systemic disturbances such as vitamin C deficiency and blood dyscrasias.

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Chapter XIV

PERITONEUM AND RETROPERITONEUM

EMBRYOLOGY

In the third week of embryonic life the extra-embryonic mesoderm is separated into somatic and splanchnic layers by a cleft which forms the initial body or celomic cavity. In the fourth week, the mesoderm of the embryo proper is divided into somatic and splanchnic layers by similar small clefts. Coalescence of the clefts starts cephally and extends caudally to form first a continuous space. By interposition of the septum transversum, the pleuro-pericardial membranes and the pleuro-peritoneal membranes the original celom is divided into the pericardial, pleural and peritoneal cavities.

ANATOMY

The *peritoneal cavity* is the largest of the serous cavities in the body. In the male it is a closed space but in the female it communicates with the exterior by means of the fallopian tubes. It is divided into two parts, (1) the *greater sac* or main portion and (2) the *lesser sac* or the omental bursa which lies between the stomach and the pancreas. The *epiploic foramen* (Winslow) connects these two cavities. Reflections of the peritoneum over patent or obliterated vessels and projecting spans from organ to organ form numerous ligaments (too many to be described here), and these are usually associated with actual or potential pouches or diverticula. *Histologically*, the peritoneum is similar to the pleura and pericardium. It is composed of an inner layer of flat cells called the *mesothelium* and an outer portion of loose connective tissue wherein are fat cells, blood and lymphatic vessels, macrophages and nerves.

PATHOLOGY

Congenital Anomalies—Developmental abnormalities of the peritoneum may be briefly considered under three headings: (1) adhesions (2) anomalies at the umbilicus and (3) hernias.

Adhesions of a congenital nature are common in fetuses. They affect both sexes and are said by some to be due to intra-uterine peritonitis and by others to represent unabsorbed peritoneal folds. The *locations* in order of frequency are the right upper quadrant, right lower quadrant and the left upper quadrant of the abdominal cavity. The *organs* involved are gall bladder to duodenum to transverse colon, gall bladder to transverse colon, gall bladder to duodenum, appendix to peritoneum, omentum to ascending and transverse colons, ascending to transverse colons and duodenum to peritoneum. *Clinically*, congenital peritoneal bands are important because they may produce obstruction to a hollow viscus and because they may form the fulcrum for a volvulus.

Anomalies at the umbilicus are infrequent. The important lesions are divisible into the following three categories: (1) those concerned with the *intestine*. They comprise an omphalocele and abnormalities of the vitelline duct—both of which have been discussed in more detail in Chapter XI; (2) those concerned with the *urachus*. These are described in the section on the urinary system; (3) *endometriosis*. The latter is uncommon. In this region, it probably arises as a metaplasia of misplaced celomic epithelium. The disorder is manifest by small bluish tinged nodules often located near the skin. They increase in size and tenderness at the time of menses and occasionally may rupture through skin with resulting hemorrhage. They are eradicated by local excision or by artificial or natural castration.

Hernia is a protrusion of any viscus or tissue through an abnormal opening of its naturally containing cavity. The *causes* of abdominal hernias are *predisposing* and *exciting*. The former are present in the form of an existing congenital sac or of a potential weak spot, and are contributed to by such factors as the following: (1) *Heredity* in 25 per cent of cases. (2) *Age*. The peak incidence occurs during the first two years of life and from fifteen to fifty years. (3) *Sex*. Males develop inguinal hernia nine times as often as females, and females develop femoral hernia three times as frequently as males. (4) *Obesity*. This increases the intra-abdominal tension and results in relaxation, atony and separation of muscles particularly those of the anterior abdominal wall. (5) *Pregnancy* also causes atrophy and separation of the muscles around the umbilicus. *Exciting* causes are those which increase intra-abdominal tension such as coughing, lifting, blow, fall or crushing injury. Although hernias are variously classified, a useful designation is one that anatomically localizes the lesions such as inguinal, umbilical etc. and then further specifies the contents and the condition of the contents.

A hernia *consists of* (1) a sac formed from peritoneum and divided into a mouth, neck and body, (2) contents which may be composed of any organ within the abdominal cavity and (3) a covering for the sac which varies, but often is composed of skin and connective tissue. The *sites* of abdominal hernias in decreasing order of frequency are inguinal, femoral, umbilical, ventral, diaphragmatic, oblique, sciatic, lumbar, perineal and internal. By internal is meant one of the nine fossas resulting from the numerous folds of peritoneum around the duodenum. Ordinarily, hernias are reducible, that is, they can be emptied of their contents at will with no discomfort to the patient and the only symptoms they produce are swelling and an annoying discomfort. If left untreated, however, most of them will in time develop *complications*. These consist of (1) *irreducibility*, that is, an inability to return the contents into the abdominal cavity. The causes are adhesions, excessive deposition of fat (as in the omentum) accumulation of intestinal contents and narrowing of the neck, (2) *inflammation* caused by irritation from a truss, accidental blow, attempts at reduction, and extension from another organ, (3) *obstruction* or *incarceration* when the lumen of the intestine is occluded by accumulation of feces and gas but the blood remains

intact and (4) *strangulation*. This is the most serious complication and consists of partial or complete vascular occlusion by pressure upon the contents of the sac by the hernial ring. Initially, the veins are affected resulting in serous and then bloody effusion. Then in quick succession, there are severe bright red to purple congestion, inflammation, ulceration of the mucosa and, in as few as five hours, gangrene of the entire loop. There is always obstruction of the bowel, and this is indicated at the mouth of the hernia by a distended afferent segment and a collapsed efferent limb of the gut (Fig. 309). If left untreated and the patient still survives, there is rupture into the sac followed by infection, abscess, break in the skin and fecal fistula.

The universally accepted and most effective treatment of hernia is surgical repair of the anatomic defect. In non-strangulated cases,



FIG. 309.—Incisional hernia from the peritoneal surface. The proximal loop of small bowel is greatly distended and hemorrhagic. The distal loop is collapsed.

the mortality rate is less than 1 per cent. In strangulated cases, it is 5 per cent if the patient is operated upon within twelve hours and it increases to 25 per cent if the operation is withheld forty-eight hours. If for some reason operation is not possible, good palliative results are often obtainable with a truss. Finally, it should also be stated that in certain selected cases obliteration of the hernial neck is possible by the injection of a sclerosing fluid, such as quinine urea hydrochloride.

Inflammations—Inflammation of the peritoneum is called *peritonitis*. It may be divided into acute non-specific and chronic specific or *granulomatous*. The latter consists of tuberculous, syphilitic, rheumatic, actinomycotic, tularemia and foreign body reactions. Foreign bodies include animal parasites (*entameba histolytica*, *oxyuris vermicularis*, *ascaris ova*, chitinous membrane of *echinococcus* cysts, and *schistosoma ova*), extravasated blood,

gelatinous substances from ovaries and appendix, oily or fatty substances (petrolatum, mucilage, gum arabic, paraffin, lanolin, gelatine agar, material from a ruptured dermoid, and fatty material from trypsin and lipase digestion in pancreatic necrosis), food particles from rupture of the stomach, lycopodium, and talcum powder. Many of the granulomas are extremely rare and, therefore, will not be considered. The following infections alone will be discussed further; (1) acute nonspecific, (2) tuberculous, (3) lycopodium and (4) talcum powder.

Acute Non-specific Peritonitis.—This is one of the most common and most important infections that confronts a surgeon. The disease may be divided into two types—primary and secondary. *Primary peritonitis* is by far the less common. It is usually caused by the pneumococcus, occurs frequently in children, particularly between the ages of two and five years, is often a terminal event in the nephrotic stage of glomerulonephritis, predominates in females and is attended by a mortality rate that is recorded as varying from 13 to 100 per cent. *The route of infection* is not agreed upon. Some maintain that it is hematogenous since there is often an accompanying upper respiratory infection; others point to the vaginal tract because the disease predominates in females and is frequently associated with a pneumococcic vulvo-vaginitis, and still others say that the presence of diarrhea and tenderness in the right lower quadrant which are often noted, indicate that the gastrointestinal tract is the portal of entry. If a correct clinical diagnosis can be made, *treatment* is non-operative and consists of the administration of sulfonamides, antibiotics and serum. In many cases, however, the condition is undiagnosed and an appendectomy is performed.

Secondary peritonitis is common. Its usual causes are the ordinary pyogenic bacteria which include *B. coli*, streptococci, staphylococci, pneumococci and gonococci. Its less frequent causes are chemicals such as bile, pancreatic juice, urine and chyle. The sources of the causative agents are the walls of the peritoneal cavity including the diaphragm and any of the abdominal organs especially the gastrointestinal tract, gall bladder, urinary system and female genital system. In each of these areas or organs the particular pathologic process responsible for the infection may be considered under the four general headings used throughout this text, namely, congenital (defects and diseases which predispose to rupture), inflammations, neoplasms (particularly ulcerating and perforating carcinomas) and mechanical factors (operations, hernia, volvulus, direct trauma, etc.). More specifically, the most common *predisposing factors* are acute appendicitis, operations on the abdomen, and tubo-ovarian infections. Secondary peritonitis affects both males and females and is found at all ages. *Symptoms and signs* may appear suddenly or insidiously. They consist of abdominal pain, nausea, vomiting, constipation, hiccoughs, abdominal tenderness, muscle rigidity, distention, tympanitis, absence of peristalsis, shallow thoracic breathing, small thready pulse, fever, leukocytosis to 20,000 per cubic millimeter, hippocratic facies (drawn face, tense anxious expression and dehydration) and finally delirium.

Pathologically, the process may be localized or diffuse. In each there are three phases which follow in rapid succession and are in effect the stages of any acute inflammation. The *stages* may not always be apparent, however, because the age of the infection usually differs in different parts of the peritoneum. The *first* stage is hyperemia. The potential capillaries, which are numerous beneath the mesothelium, dilate, become engorged and thereby produce a pinkish blush. Initially, the circulation is speeded up but as the leukocytes adhere to the walls it is slowed. Soon leukocytes and serum escape into the adjoining loose connective tissue and are later followed by extravasation of erythrocytes. Concomitantly, the peritoneal surface loses its luster. The *second* stage is one of exudation. Diapedesis of leukocytes and erythrocytes and escape of plasma continues into the areolar connective tissue and upon the



FIG. 310.—Recent adhesions from a case of postoperative peritonitis

mesothelial surface, and is seen grossly as pus. The character of the latter varies according to the relative proportions of serum, fibrin, leukocytes and erythrocytes and may thus be serous, fibrinous, purulent, hemorrhagic or any combinations of these. In mixed infections, it is not distinctive but in single infections, it may be characteristic. That caused by pneumococci, for example, is thick and fibrinopurulent, that by streptococci, thin watery turbid and flecked, and that by gonococci, thick and creamy. The *third* stage is the plastic or adhesive stage. Adjoining serosal surfaces being covered with an exudate are joined together. This is a protective mechanism which tends to localize and wall off the infection. Accordingly, large or small single or multiple pockets of pus are formed between loops of intestine, surfaces of other organs, the parietal peritoneum and the omentum. Initially, the adherent surfaces are loosely attached and easily separated. Later, some of

gelatinous substances from ovaries and appendix, oily or fatty substances (petrolatum, mucilage, gum arabic, paraffin, lanolin, gelative agar, material from a rupture dermoid, and fatty material from trypsin and lipase digestion in pancreatic necrosis), food particles from rupture of the stomach, lycopodium, and talcum powder. Many of the granulomas are extremely rare and, therefore, will not be considered. The following infections alone will be discussed further; (1) acute nonspecific, (2) tuberculous, (3) lycopodium and (4) talcum powder.

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of general anti-tuberculosis measures, of antibiotics, and in the ascitic form, of laparotomy with removal of as much fluid as possible. If the primary focus in the fallopian tube or cecum is found, it should be removed. Because the diagnosis is now made sooner than it was formerly, the prognosis is more favorable. Death is usually due to pulmonary tuberculosis.

Lycopodium Granuloma—Lycopodium granuloma of the peritoneum is caused by spores of lycopodium which are found in a dusting powder used on the surgeon's gloves. It occurs in people previously operated upon. The lesion consists of adhesions in which there are numerous pearly white nodules that resemble tubercles. *Histologically*, the granuloma is composed of pseudotubercles disclosing central areas of necrosis surrounded by epithelioid cells, round cells and foreign body giant cells. The sup-

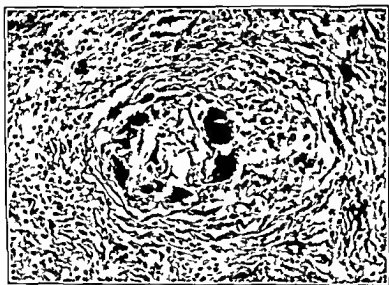


FIG. 311—Talcum powder granuloma showing a pseudotubercle composed of foreign body giant cells surrounded by epithelioid cells. $\times 100$

porting stroma is fibrous. The most distinctive features are the spores. They are present within the granulation tissue and within the giant cells and are best discernible by the Ziehl-Neelsen stain. They are spheroidal bodies 30 microns in diameter and disclose a scalloped contour due to short peripheral spinous processes. The centers of some are empty, while those of others are filled with granular material.

Talcum Powder Granuloma—This is a reaction of the peritoneum to magnesium silicate crystals which are used as dusting powder for rubber gloves. This is one of the most common causes of post-operative adhesions and yet, despite this knowledge, few surgeons have discarded its use. The source of the powder is the outsides of the gloves that are not correctly washed and ruptured finger tips where it often collects. *Grossly*, the lesions consist of fibrous adhesions wherein tiny nodules are frequently located. *Histologically*,

the exudate is resorbed while some becomes organized into loose and thin dense fibrous tissue thus forming the well-known peritoneal adhesions (Fig. 310).

The *diagnosis* of acute peritonitis is easy when the process originates abruptly, but may be extremely difficult when it arises insidiously, especially when the patient is already ill from another disease. So many factors enter into the *treatment* and *prognosis* that blanket statements in this regard can scarcely be made. In general, however, it may be stated that the causative factors should be eliminated as soon as possible, that is, a ruptured appendix should be removed, a perforated ulcer closed, a strangulated hernia released and resected, etc. It may also be stated that chemotherapy and antibiotics as additional measures have practically revolutionized the treatment of acute peritonitis and have reduced the mortality rates immeasurably.

Tuberculous Peritonitis.—This inflammation has been recorded as occurring in about 10 per cent of all patients dying from tuberculosis, and is superceded as a cause of death in this disease only by infection of the lungs and intestines. The tubercle bacilli usually gain *entrance* directly from lesions in retroperitoneal or mesenteric lymph nodes, the bowel, or the fallopian tubes, and are blood borne only in cases of miliary tuberculosis. Primary infection of the peritoneum probably does not occur. The disease affects both males and females (usually of the poorer classes) and although it is found at all ages, it predominates in young and middle aged adults. *Symptoms* and *signs* are, as a rule, insidious and consist of vague inconstant abdominal pain, gradual increase in size of the abdomen, spells of nausea and vomiting, headache, malaise, fever, loss of weight, pallor and abdominal tenderness. Less often the onset is acute and is manifested by sudden abdominal pain, vomiting, tenderness, fever to 104°F, increase rate of pulse and respirations, and lack of leukocytosis.

The disease may appear in one of the following *three forms*. (1) *Ascitic*. In this type the peritoneal cavity is distended with yellowish fluid that is low in fibrin and that has a specific gravity of about 1.020. The serosal surfaces are covered with small tubercles, are usually red, and less often are strewn with fibrin. In addition the primary focus in the lymph nodes, bowel or adnexia may be apparent. (2) *Adhesive*. In this type the free fluid is in abeyance; fibrin is prominent; the exudate is gelatinous, greenish and collected in pockets; the underlying tubercles are obscured; the opposing loops of bowel are plastered together and often obstructed first by the exudate and later by fibrinous and fibrous adhesions, and the omentum is infiltrated and shortened to form a transverse roll. (3) *Caseous*. This is essentially similar to the adhesive type with the exception that caseation is added. *Histologically*, the lesions are similar to those in other organs.

The *diagnosis* of tuberculous peritonitis is difficult primarily because the condition is relatively uncommon. It should be suspected in any patient known to have or have had tuberculosis who presents symptoms and signs pointing to the abdomen. *Treatment* consists

peritoneal tumors are those of connective tissue origin especially lipomas, that the most common malignant neoplasms of the retroperitoneum are lymphoblastomas and of the peritoneum secondary cancers, that the growths are usually limited to the abdominal cavity, and that metastases most often to the liver, lungs and lymph nodes but also to any other parts of the body are recorded in from 37 to 30 per cent of all cases.

Clinically, peritoneal and retroperitoneal tumors occur at all ages with a preponderance in the fourth and fifth decades, and they are more frequent (particularly fatty tumors) in women than in men. The most common initial *symptom* is swelling of the abdomen due to either the tumor or the accompanying ascites or both. When complications arise such as intestinal obstruction, pressure on a ureter, torsion, rupture or peritonitis the symptoms and signs vary accordingly. There are usually pain, constipation, nausea and vomiting, abdominal tenderness and a palpable mass in 75 per cent of the cases. The *diagnosis* is made on the basis of exclusion. It is materially aided by simple roentgenograms of the abdomen, by retrograde urograms and by barium studies of the gastro-intestinal tract. A precise diagnosis, however, is established, as a rule, after exploratory laparotomy and then usually with the aid of a biopsy. Clinically, omental and retroperitoneal tumors are confused with neoplasms of any of the abdominal viscera especially the ovaries, kidneys and gastro-intestinal tract. *Treatment* is surgical enucleation for all but the lymphoblastomas, when irradiation should be employed. The *prognosis* is unfavorable because the growths are usually attached to vital structures at the time of operation and cannot be completely extirpated. It is of course worse in malignant tumors than in benign ones. The immediate *operative mortality* from shock is recorded as varying from 16 to 25 per cent.

Aside from the above general considerations, three processes that are not considered elsewhere and, therefore, merit a few additional remarks are secondary cancer of the peritoneum, pseudomyxoma of the peritoneum and ecchinococcus cyst.

Secondary cancer of the peritoneum—This exceeds all other neoplasms of the abdominal cavity. Although the primary lesions can occur anywhere in the body, carcinoma of the stomach and ovary are the most frequent offenders. The *routes of invasion* are three: (1) direct extension from the involved organ through the visceral peritoneum or metastasis to regional nodes, and then penetration of the serosa secondarily, (2) implantation. This is especially true of ovarian carcinoma where the tumor penetrates the capsule grows on the surface and breaks off or where the capsule ruptures and the contents are seeded all over the celom, (3) blood borne metastases. These usually occur in conjunction with generalized dissemination throughout the body. *Grossly*, the lesions are quite variable. Sometimes, they are limited to a small area opposite the primary tumor while at other times, they cover all the serosal surfaces. The omentum, as a rule, participates in the latter to form a rolled or bunched mass of neoplastic infiltrate. The nodules vary in size from a millimeter to 1 or 2 cm, but some-

they are composed of collections of lymphocytes, epithelioid cells and foreign body giant cells (Fig. 311). Crystals of magnesium silicate may be seen with ordinary lenses, but they become particularly conspicuous when viewed with the aid of crossed Nicol prisms. They are scattered throughout the tissue and within giant cells. The greatest danger of adhesions is, of course, intestinal obstruction and once this occurs, the only *treatment* is surgical lysis. Since they reform repeatedly, the final outcome may be serious. The best treatment, therefore, is prophylaxis. Talcum powder should be condemned as dusting powder and replaced by more innocuous substances, such as potassium bitartrate.

Tumors.—On a histogenetic basis neoplasms of the *peritoneum* and *retroperitoneum* may be classified as follows: from mesothelium, mesothelioma; from connective tissue, fibroma, fibrosarcoma, myxoma and myxosarcoma; from fat, lipoma and liposarcoma; from nerve tissue, neurofibroma, neurofibrosarcoma, sympathoblastoma (neuroblastoma), ganglioneuroma, and pheochromoblastoma; from vessels, hemangioma and lymphangioma (chylous cyst); from lymph nodes, lymphoblastoma which among others includes lymphosarcoma, Hodgkin's disease, reticulum cell sarcoma and giant follicular lymphoblastoma; from muscle, leiomyoma, leiomyosarcoma and myosarcoma; from the urogenital cell ridge, dermoid, teratoma and chorionepithelioma; from mesodermal elements as a result of metaplasia, osteochondrosarcoma; from distant areas, secondary cancer, endometrioses, abdominal pregnancy, lithopedium and pseudomyxoma of the peritoneum, and an inflammatory swelling but not a true tumor—ecchinococcus cyst. Since the *omentum* is less complex in composition than the retroperitoneum the tumors are less varied. Some of the more commonly described growths are: from connective tissue, fibroma, fibrosarcoma, myxoma, and myxosarcoma; from vascular tissue, hemangioma, hemangio-endothelioma and lymphangioma (chylous cyst); from fat tissue, liposarcoma, and from distant areas metastatic cancers.

Because most of these neoplasms are adequately discussed from the gross and microscopic standpoints in other portions of the text, there is no need of repeating the descriptions here. Thus tumors of connective, fatty and vascular tissue are considered in the section on the skin (p. 9); dermoids, teratoma and nerve tissue tumors are discussed in the chapter on the mediastinum (p. 244); leiomyoma and leiomyosarcoma are described in the sections on the stomach and uterus (p. 332 and 587), lymphoblastomas are considered in connection with lymph nodes (p. 484); mesothelioma is similar to mesothelioma of the pleura, etc. *In general*, it may be stated that the tumors are cystic or solid depending upon their histogenesis; that they occasionally contain calcareous material or bone; that they usually grow to large proportions (to 60 pounds in weight); that they produce symptoms by pressure upon adjacent structures and organs, by torsion and infarction (particularly omental growths), by erosion of vessels and internal hemorrhage, or by rupture and production of peritonitis; that the most common benign retro-

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included here only because it presents as a cystic swelling that may be confused with a neoplasm. Apart from man, cysts are found in sheep, cattle and pigs. These are eaten by the dog and the wolf, and, thus, in their intestines the adult worm develops. Ova are discharged in the feces, reach the digestive tract of man (or sheep, cattle and pigs), lose their membrane and liberate an embryo which penetrates the intestine and then wanders off to form the cyst. The cyst grows slowly, until ultimately it reaches a diameter of 15 cm. or more. The wall is pearly white, chitinous and measures as much as 1 cm. across (Fig. 312). Its inner surface is called the brood membrane and gives rise to larvae and daughter cysts. When the larvae degenerate, the hooklets which they bear are scattered throughout the fluid. Clinically, echinococcus cysts may reach large sizes and may be entirely silent. Symptoms when present



Fig. 312 —Echinococcus cyst of the liver containing fragments of daughter cysts

are those of a tumor and, of course, vary according to the organ or tissues involved. The diagnosis is made from cutaneous sensitivity, precipitin test, complement fixation test, the chitinous appearance of the cyst wall, and finding of hooklets and scolices in the fluid of the cyst. Treatment of pedunculated cysts is excision, whereas of calcified, thin and embedded cysts, it consists of sucking out the contents and destroying the brood membrane. If the material is spilled and the larvae are living, new cysts will develop at the sites of implantation. The prognosis is guarded.

Mechanical Disturbances —Under this heading will be considered (1) adhesions, (2) trauma, (3) foreign bodies, (4) torsion of the omentum and (5) infarction of the omentum.

Adhesions —Adhesions in the peritoneal cavity are said to occur in 90 per cent of previously laparotomized patients and to account for 3.5 per cent of all abdominal operations performed for intestinal

times they are uniformly minute and may then be mistaken for tubercles. Careful inspection, however, often shows central umbilication and smoother surfaces—features not found in tuberculosis. In most cases of peritoneal carcinomatosis the serosa reacts with the formation of fibrin and an outpouring of straw-colored or sanguineous serum. In a few, when the primary tumor is a colloid carcinoma, the celom is filled with massive mucoid material that resembles pseudomyxoma of the peritoneum. *Histologically*, the growths resemble the parent neoplasm. Clinically, *symptoms*, when present, usually consist of an enlargement of the abdomen and less often, they are those of intestinal obstruction. The *diagnosis* is established by identifying neoplastic cells in the sediment of ascitic fluid, by peritoneoscopy when the lesions are visualized and a biopsy secured, and at laparotomy. The *prognosis* is poor.

Pseudomyxoma of the Peritoneum.—This is an uncommon condition that usually results from rupture of a pseudomucinous cystadenoma or cystadenocarcinoma of the ovary, and less often from rupture of a mucocele of the appendix. The *nature* of the *process* is not agreed upon. Some authors say that cells from the ruptured organ are disseminated throughout the peritoneal cavity, become implanted on the serosal surface, continue to secrete mucoid material, and are, therefore, in effect cancerous. Others maintain that the sudden spreading of the contents throughout the peritoneum induces a low grade chemical peritonitis wherein the mesothelium is transformed into columnar epithelium and is responsible for the continued outpouring of fluid. At any rate, the *celom* is usually filled with gallons of mucoid exudate that is often referred to as resembling frog spawn or fish eggs, and the serosal surfaces of the gut are agglutinated to themselves, to the omentum and to other abdominal viscera. Adherent to the peritoneum there are yellowish, grey or pearly white globular masses of varying sizes. These are composed of a capsule of fibrous tissue from which trabeculations are sent centrally and break up the mass into numerous small cysts. The latter are filled with mucoid material admixed with cellular debris and leukocytes. At the periphery, there may be scattered strands of columnar epithelium and beyond these, there are lymphocytes, plasma cells, eosinophils, histiocyte and foreign body giant cells. The tissue between the cysts is often myxomatous. *Clinically*, the usual manifestation is a painless distention of the abdomen. Terminally, there are loss of weight, anorexia and intestinal obstruction. *Treatment* consists of removing the source of the condition, that is, the ovarian or appendical lesion and scooping out as much of the exudate as possible. The ultimate *prognosis* is ordinarily poor. The *causes of death* are intestinal obstruction, inability of the celom to cope with infection and infarction of the small bowel from compression of the portal circulation.

Echinococcus cysts.—These are also known as hydatid disease and may be found in the mesentery, retroperitoneum, liver, lungs and other tissues and organs of the body. The lesion represents the larval stage of taenia ecchinococcus, is not a true tumor and is

swallowed and then perforating the gastrointestinal tract. By far the most common and most important from a medicolegal standpoint are objects left behind at the time of operation. These include sponges, forceps, clamps, hemostats, scissors, towel clips, retractor, blades, pieces of instruments, anastomosis buttons, catheters, needles, diamond ring, etc. The damage produced depends upon the location, size, sharpness, irregularity, sterility, and hardness of the object. The *pathologic change* evoked consists of (1) infection resulting in abscess formation, (2) aseptic irritation which produces exudation and encapsulation of the object, (3) pressure erosion of an adjacent structure and (4) a tendency to extrusion where the resistance is least. *Treatment* consists of (1) prevention and (2) removal. The *prognosis* is good.

Torsion of the Omentum—This is idiopathic in origin or is caused by hernia, by adhesions, by deformity of omentum as seen in tumors or irregular deposition of fat, and by intraperitoneal inflammations. The force required is supplied by intestinal peristalsis, by action of the diaphragm and muscles of the abdominal wall, by blows to the abdomen and by sudden body movements. The torsion may be segmental or involve the entire organ and either partial or complete. It affects males more frequently than females, and usually occurs between the ages of thirty to fifty-five years. The most common *symptom* is gradually increasing right sided abdominal pain and the most common clinical diagnosis is appendicitis. *Treatment* at the time of laparotomy is surgical excision. The *prognosis* is good.

Infarction of the Omentum—Infarction of the omentum of unknown cause is rare. Usually a *terminal segment* of the right side of the omentum is involved. It is deep red to black, swollen, firm, friable and sharply demarcated from normal tissue. The peritoneal cavity contains an excess serosanguineous fluid. *Histologically*, there are recent thrombi of the veins, erythrocytic extravasation into the adjacent fat and an infiltration with monocytes, plasma cells, neutrophils and macrophages. *Clinically*, symptoms arise suddenly and consist of pain in the right lower quadrant of the abdomen, nausea, vomiting, constipation and leukocytosis to 18,000 per cubic millimeter of blood. The condition is, therefore, rightfully mistaken for appendicitis. *Treatment* at the time of operation is surgical excision. The *prognosis* is good.

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obstruction. The condition is, therefore, common and sometimes serious. The *causes* of adhesions are (1) an inherent tendency of some individuals to respond to injury more vigorously than others, (2) injury to serosa at the time of surgical operation due to chemicals (talcum powder), heat, foreign bodies (sutures), ecchymosis, sepsis and rough handling of tissue, (3) disease processes such as inflammations (peritonitis) and (4) external trauma. Although post-operative adhesions are common, only a minority produce *symptoms*. These may be due to a reflex mechanism and consist of abdominal distress, nausea, regurgitation and vomiting, to intestinal obstruction and to traction upon the parietal peritoneum by contraction of scar tissue. *Pathologically*, damaged peritoneum reacts by exudation of fibrin. If the mesothelium is intact or if the serosal cells alone are injured, the fibrin and débris are ultimately removed by phagocytosis, the lining cells are restored and resolution is complete. If the mesothelium and submesothelial connective tissue are damaged, the fibrin becomes infiltrated with adjacent fibroblasts and is converted successively into granulation, connective and thin fibrous tissue to form a permanent adhesion. *Treatment* has been directed towards (1) prevention by eliminating the causes already enumerated, (2) keeping apart the injured surfaces by various means, (3) dissolving fibrin by means of ferments, (4) preventing coagulation of peritoneal exudate by the use of anticoagulants such as heparin and (5) surgical intervention—lysis. The usual indication for the latter is obstruction to a viscus, most commonly the intestinal tract. Nor is it always successful, for often successive operations are followed by an alarming and progressive increase of adhesions. The *prognosis*, once symptoms are produced, must, therefore, be guarded.

Trauma.—Trauma to the peritoneum and abdominal viscera may be classified as (1) *penetrating*—due to shotgun, pistol, rifle or stab wounds and dynamite caps and (2) *non-penetrating*—due to blows or crushing injury. In these cases a viscus may be injured by impingement, tearing because of a tangential force, gas and fluid within the organ or penetration of bony spicules. Any organ or combinations of organs may be affected and the injury may be trivial or severe. *Symptoms* range from none to abdominal pain (due to peritoneal irritation) and severe shock (from massive hemorrhage). The extent of injury particularly in non-penetrating wounds is sometimes difficult to ascertain. Such patients should, therefore, be closely observed. Most penetrating wounds are explored early and the damage repaired. Although sulfonamides and antibiotics have been of great value, the mortality rates for penetrative wounds are still recorded in the neighborhood of 50 per cent. The immediate *causes of death* are shock and hemorrhage, whereas later causes are pneumonia and peritonitis. The *prognosis* depends upon the extent of injury, time interval between sustaining the injury and treatment, loss of blood and shock.

Foreign Bodies.—These gain *entrance* into the peritoneum by (1) being left behind at the time of operation, (2) being accidentally introduced from the outside at the time of an accident and (3) being

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for gall bladder, right posterior for inferior vena cava, and transversely in the center the *porta hepatis* for transit of vessels, nerves and bile ducts. The lobes number four—left, right, quadrate (central anterior and inferior) and caudate (central and posterior). The *falciform ligament* connects the liver with the diaphragm and anterior abdominal wall. Along its free border courses the obliterated left umbilical vein. The portal vein, hepatic arteries and nerves (sympathetic and left vagus) enter the liver at the *porta hepatis*, and the bile ducts and lymphatic leave through the same portal. The latter empty into the nodes along the inferior vena cava. The venous return from the liver is by way of the hepatic veins and they drain directly into the vena cava.

The *histological unit* is the lobule—a polygonal prism 0.7 to 2 mm in diameter (Fig. 313). Its hub contains the central vein which

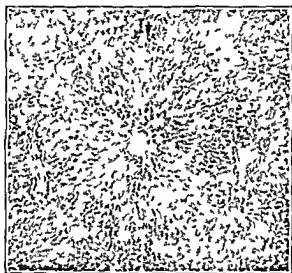


FIG. 313.—Normal hepatic lobule showing a central vein radiating cords and peripheral portal radicles. $\times 375$

unites with other veins to form collecting veins, and these in turn form the hepatic veins. Between the lobules invested in connective tissue are branches of the portal vein and hepatic arteries, bile ducts and lymphatics. Between these portal radicles are hepatic cords arranged in a radiating manner from the center. Their cells are polygonal, have one or occasionally two vesicular nuclei and an abundant amount of eosinophilic cytoplasm which however is variable because of the labile glycogen and fat content. The cords are composed of two rows of cells between which are bile canaliculi. These unite and ultimately form the interlobular bile ducts. Separating the cords are sinusoids which connect the portal and central veins, and receive blood from the hepatic arteries. They are lined by large phagocytic cells of von Kuppfer (reticulo-endothelial), the cytoplasm of which frequently contains green pigment.

Chapter XV

LIVER, BILIARY SYSTEM AND PANCREAS

LIVER

EMBRYOLOGY

THE liver and biliary system first become apparent in the 3 mm. embryo as a hepatic diverticulum that bulges from the floor of what later forms the duodenum. The cranial part of the sacculation forms the glandular tissue and bile ducts, while the caudal part gives rise to the gall bladder and cystic duct. The *glandular portion* arises as budding epithelial cords which invade the septum transversum and receive the vitelline veins. Between the cords sinusoids are formed and within the perisinusoidal spaces active hemopoiesis is apparent from the second month of embryonic life till birth. Dovetailing of the portal and hepatic veins forms the hepatic lobules. Single at first, these continue to multiply until at birth they number in thousands. The radiating pattern of cords, however, is not established until early childhood. The *biliary system* is initially solid. The common bile duct (ductus choledochus) and hepatic ducts arise from the main portion of the diverticulum; the larger intrahepatic ducts develop as branches from the expanded end of the hepatic duct, while the interlobular ducts arise from liver cords. The *gall bladder* originates as a solid cylinder from the caudal portion of the diverticulum but soon elongates to form a connecting cystic duct. As the liver expands, it grows caudally from the septum transversum to form a bulky mass that is ultimately attached to the original septum (the diaphragm) by a fold of the ventral mesentery called the *falciform ligament*. The visceral peritoneum comes from the covering of the system transversum and the connective tissue and muscles of the biliary system develop from mesenchyme.

ANATOMY

The *liver* occupies the right hypochondrium, most of the epigastrium and part of the left hypochondrium. It weighs about 1650 gm. and its greatest diameters measure as follows: transverse 15 to 20 cm., vertical 15 to 17 cm. and antero-posterior 12 to 15 cm. The organ is firm friable and dark reddish brown. Its relations are: superior, anterior and right lateral surfaces covered by diaphragm, posterior surface resting in its central portion on the vertebral bodies and crura of the diaphragm, and inferior surface in contact with the stomach, duodenum, lesser omentum, hepatic flexure of the colon, and right kidney. There are five *fossas* in the central portion of the inferior and posterior surfaces: left anterior for umbilical vein, left posterior for ductus and later legamentum venosum, right anterior

dense fibrous tissue and within the latter, there are often distorted and proliferated bile ducts

Cysts of the liver are important chiefly because they may form irregularities that by palpation are considered to represent a more serious disease. If they produce no symptoms and the abdomen is opened because of a mistaken diagnosis, they should be left alone, if they are deeply situated, but they may be excised, if they are pedunculated. If they produce symptoms, those that protrude may be excised, while others may be incised and drained. The prognosis is generally good, but it may be poor if both kidneys are involved by a similar process.

Inflammations—Inflammatory lesions of the liver of surgical importance are pyogenic abscess, amebic abscess, *Echinococcus* cyst, syphilis, tuberculosis, and cirrhosis. *Echinococcus* disease has been considered in the preceding chapter and will be omitted here.

Pyogenic Abscess—This abscess of the liver is caused by pyogenic organisms which most often consist of the colon group, streptococci and staphylococci and less often of Friedländer's bacillus, pneumococci, fecal bacilli, etc. It is said that in as many as 50 per cent of cases the source of the infection is acute appendicitis that is followed by *pylephlebitis*. The latter is initially an inflammation of the terminal branches of the ileo-colic vein. If the involved radicals are not removed at the time of appendectomy, the infection spreads to the larger branches by contiguity, or portions of septic thrombi that form rapidly are broken off and are carried to the liver. In addition to inflammation of the appendix, the portal vein may convey infected material to the liver from infected thrombotic hemorrhoids, diverticulitis or pelvic inflammatory disease. Other sources and routes of infection are (1) hematogenous by way of hepatic arteries in cases of osteomyelitis, furunculosis, pyemia etc., (2) along the bile ducts from cholecystitis, small intestine and obstruction of the biliary tract, (3) contiguity from cholecystitis, subdiaphragmatic abscess, empyema and perinephric abscess, (4) trauma from penetrating injury or contusion and (5) idiopathic. In approximate order of frequency, *symptoms* and *signs* of hepatic abscess are fever, chills, right upper quadrant pain, profuse sweating, nausea, vomiting, tenderness over the liver, leukocytosis, elevation and immobility of the diaphragm and basilar atelectasis (roentgenographically), and, terminally, jaundice.

The location of the lesions in the liver depends upon the route of infection. If the latter is by contiguity, the site will be opposite the diseased organ or tissue, if by the hepatic arteries or the biliary tree, it will be diffuse, and if by the portal vein, it will depend upon the primary lesion. If this is in the area drained by the superior mesenteric vein, the right lobe of the liver will be affected while if in the area drained by the inferior mesenteric vein, the left lobe will be involved. The abscesses may be single but, as a rule, they are multiple and if the latter they usually measure as much as 1 cm. in diameter. The liver is ordinarily enlarged. If the lesions are superficial, the surface is irregular and rather soft whereas if they

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the liver consist of *hypoplasia* or *hyperplasia* of the lobes (a tongue-like enlargement of the right lobe posteriorly which is known as *Riedel's lobe* and may be confused with the kidney), an *absence* of a lobe or of the entire liver, *transposition* of the liver as seen in *situs transversus*, *cysts* and *hypoplasia* of the portal system. The latter is associated with a normal or small liver, portal hypertension, distention of abdominal veins accompanied by a venous thrill and murmur, and persistent leukopenia. This symptom complex is known as the *Cruveilhier-Baumgarten disease* and is to be distinguished from a similarly named syndrome which is caused by portal hypertension resulting from hepatic cirrhosis, portal thrombosis or Banti's disease.

Cysts.—Non-parasitic cysts of the liver may be single or multiple. The latter are also *known* as congenital cysts, polycystic disease of the liver, cystic disease, cystic degeneration of the liver and cystic liver. Some authors say that single cysts develop from multiple cysts as a result of breakdown of the intervening walls. Others say that they result from local obstruction of the biliary tract. The *origin* of multiple cysts has been attributed to (1) inflammation about the ducts causing obstruction of the latter, stasis and retention, (2) congenital obstruction of the biliary ducts, (3) degeneration of tumors as sarcoma, carcinoma and cystic adenoma, (4) a neoplasm of bile ducts—cavernous biliary angioma and (5) a persistence of a normal fetal stage that is explained as follows. Normally the first generation of bile ducts segment and then degenerate and resorb. Abnormally degeneration and resorption fails and the proliferated ducts remain to dilate and form cysts. This appears to be the most plausible interpretation and is in keeping with the formation of cysts in other organs. The incidence of cystic disease of the liver is about 0.17 per cent of all cases coming to necropsy; it predominates in males in the ratio of three to one, and although congenital it is usually discovered in the fourth decade of life. *Clinically*, the cysts are silent until they become large enough to produce pressure upon adjacent structures, when they are accompanied by symptoms referable to the stomach, gallbladder or even liver. Rupture of the cysts may result in a chemical peritonitis. When large, the dilatations may be felt through the abdominal wall as irregular bossings.

If the *cysts* are at or near the surface, the liver is usually enlarged but if they are central, an increase in size may not be apparent. As already stated, the cysts may be single or multiple and vary in size from microscopic to 15 cm. or more in diameter. The walls are thin and fibrous; externally the color is straw-like or varying shades of blue; the contents are usually watery and less often brown from old hemorrhage, and the inner surface is smooth and glistening. *Histologically*, the inner surfaces of the smaller cysts are lined with columnar, cuboidal or flat epithelium, whereas those of larger cysts are devoid of an epithelial lining. About these, there is loose or

The wall is composed of connective tissue wherein are found erythrocytes, lymphocytes, neutrophils and, at its junction with normal tissues, the vegetative organisms. With age monocytes appear, the connective tissue becomes more dense and the neutrophils disappear.

The diagnosis is established when there are fever and pain and tenderness over the liver in a known case of dysentery. Obtaining chocolate brown pus from the abscess is said to be pathognomonic. In some patients subcutaneous administration of emetine hydrochloride is curative while in others this treatment needs to be supplemented by needle aspiration or drainage. The mortality rates are reported as ranging from 3 to 20 per cent.

Tuberculosis—Tuberculosis of the liver is not a surgical problem. Tubercles are found in this organ in about 50 per cent of cases of pulmonary tuberculosis. The organisms gain entrance by the hepatic arteries in disseminated tuberculosis and by the portal vein in intestinal lesions. They may be found (1) as scattered tubercles, (2) as miliary tubercles which are diffusely distributed, measure about 1 mm in diameter and are grey or yellow, (3) as tuberculomas which are greyish white, may be several centimeters in diameter and have a tendency to become caseous and (4) as pericholangitic necrotic tuberculous abscesses.

Syphilis—Syphilis of the liver is likewise not in the domain of the surgeon, and is included here only because at laparotomy the lesions may be confused with neoplasms and other diseases. *Congenital syphilis* exists as a diffuse interlobular and intercellular fibrosis which is flooded with spirochetes. *Tertiary syphilis* is primarily *gummatous*. The lesions may be single or multiple, deeply or peripherally situated, and microscopic to 6 cm in diameter. They have no predilection for any of the lobes. Healing starts at the periphery in the form of fibrous tissue whence it extends outwardly between the hepatic lobules and inwardly to replace the gumma itself. As this tissue contracts the liver becomes greatly distorted and transformed into irregular lobes that are separated by depressed stellate scars. This is called *hepar lobatum*. A third type of tertiary lesion that is described is diffuse interstitial hepatitis or *syphilitic cirrhosis*. It is probable, however, that such hepatic changes are not caused by the spirochetes but that they merely represent an ordinary portal cirrhosis in a syphilitic patient. Syphilis of the liver is a benign disease even in the absence of specific therapy, and it rarely contributes to the death of the patient.

Cirrhosis—Cirrhosis of the liver is important to the surgeon because at laparotomy and peritoneoscopy it must be differentiated from other diseases, because one type (obstructive biliary) is directly a surgical problem and because it constitutes the most common cause of portal hypertension. It may be defined as a progressive diffuse chronic inflammatory disease of the liver associated with fibrosis and regression and regeneration of the parenchyma. Since the causes differ according to the type of cirrhosis, they will be briefly mentioned under the separate subdivisions. Generally speaking, the incidence of cirrhosis varies in different

are deep, it is smooth and rather firm. The larger abscesses show central areas of complete liquefaction filled with varying types of pus, ragged grey inner surfaces that are often bile stained, and rarely connective or fibrous tissue encapsulation. Satellite abscesses about the larger ones are often found. *Histologically*, as in other acute abscesses, the centers are filled with débris, leukocytes and nuclear fragments and the peripheries are surrounded by large or small amounts of granulation tissue.

The disease should be *suspected* when chills, fever and tender liver develop, particularly following an attack of appendicitis or appendectomy. Of diagnostic importance are elevation and immobility of the right diaphragm and basilar atelectasis of the right lung. *Treatment* consists of (1) attention to the source of the infection when that can be established, (2) antibiotic and chemotherapy and (3) drainage of the hepatic abscess only if it is localized and if signs and symptoms do not abate following drug therapy. The *complications* are: pneumonia, lung abscess, empyema, peritonitis, sub-diaphragmatic abscess and pulmonary embolism. Formerly, the *mortality* in single abscess was about 40 per cent and in multiple abscess it approached 100 per cent. With the advent of sulfonamides and later antibiotics, reports of cures are appearing in the literature so that the *prognosis* is now immeasurably improved.

Amebic Abscess.—This abscess of the liver is secondary to amebic disease of the bowel. The latter is universal in distribution and is said to occur in from 5 to 20 per cent of the population in the United States. Hepatic involvement occurs in about 5 per cent of cases of amebic colitis and is responsible for about one-third of all deaths from this disease. It is caused by the *endameba histolytica*—a protozoa that in the vegetative stage measures 20 to 40 microns in diameter. It is grey or colorless, granular, motile and is composed of a peripheral rim of ectoplasm and inner mass of endoplasm which contains contractile vacuoles, ingested erythrocytes and a round nucleus with a central karyosome. In its cystic stage, it measures 7 to 15 microns and when fully developed, it discloses four nuclei. Amebic abscess of the liver occurs in males in 85 per cent of the cases and is most prevalent between the ages of twenty and fifty years. Traumatism, alcoholism and dietary deficiencies are considered as *predisposing causes*. Hepatic involvement occurs at any time after the bowel has been infected. Symptoms and signs are similar to those of pyogenic abscess.

The *route of infection* is by way of the portal vein. The organisms lodge in a terminal radicle, produce a thrombus, cause necrosis of the wall and escape into the hepatic parenchyma where they form the *abscess*. The latter is single or multiple, is deeply or superficially situated, involves the right lobe six times more frequently than the left and measures as much as 20 cm. in diameter. The initial lesions are minute greyish brown foci with irregular edges, but as they enlarge their walls become dense and fibrous. At first the contents are mucoid and grey, but due to the extravasation of blood they later become chocolate brown in color. *Histologically*, the pus is composed of débris, nuclear fragments and leukocytes.

broad or narrow depressed bands of fibrous tissue. The color varies from brown to green, red or yellow and the consistency from soft, when the organ is enlarged, to hard, when it is atrophic. *Histologically*, the portal radicles disclose an increase of dense fibrous tissue, an infiltration with varying numbers of lymphocytes, plasma cells and neutrophils, and a proliferation of bile ducts. In the early stages, the hepatic lobules show cloudy swelling, fatty degeneration, foci of necrosis and regeneration. The latter occurs in an irregular manner to form pseudolobules wherein the radiating pattern is lost and the draining veins are eccentric in position. *Treatment* of portal cirrhosis is dietary consisting of high protein, moderate amount of fat, high carbohydrate, yeast, choline and cystine. When ascites and esophageal varices develop, surgery (which is discussed under portal hypertension) is indicated.

Pigmentary cirrhosis is known also as *hemochromatosis*. It is portal cirrhosis associated with cutaneous pigmentation, diabetes and hemosiderosis. The process has been considered as primarily diabetes which produces endarteritis in the liver resulting in hepatic damage, as primarily a derangement of the liver, as excessive hemolysis of erythrocytes with liberation of hemosiderin which eventuates in fibrosis, as hepatic damage produced by various toxic agents and consequently altered metabolism and as representing an inborn error of metabolism. From an analysis of our autopsy material and experimental alloxan diabetes in rabbits, it is our contention that alloxan or an allied substance produces both necrosis of Islets of Langerhans and periportal hepatic cells resulting in diabetes mellitus and cirrhosis, that dietary deficiencies aggravate the cirrhosis, that the consequent portal hypertension produces interlobular and intralobular fibrosis of the pancreas and that abnormal retention of iron results in hemosiderosis. The cirrhosis as already stated is of the *portal* type. Hemosiderin and hemofuscin are deposited within hepatic cells, the periportal fibrous tissue and the fibrous tissue between and within the pancreatic acini and elsewhere in the body. *Treatment* as in portal cirrhosis is correction of the avitaminosis and, in addition, attention to the diabetes.

Biliary cirrhosis is due to obstruction or inflammation of the bile ducts or both. In children, the cause is usually congenital stenosis or atresia of the bile ducts whereas in adults, it is due to obstruction by tumors, concretions or inflammation. *Grossly*, the liver is often enlarged, green, firm and finely nodular. *Histologically*, the lesion is similar to portal cirrhosis except that the fibrosis is less marked, bile duct proliferation is not conspicuous until late in the disease, whereas early there is marked dilatation with even papillary enfoldings, inflammatory cell infiltration is more severe, bile casts are found in the terminal bile passages, and the nodular proliferation of the hepatic cells is less marked. *Treatment*, of course, is elimination of the cause.

Tumors—Histogenetically, neoplasms of the liver may be enumerated as follows: from hepatic cells, an adenoma (benign hepatoma) and carcinoma (malignant hepatoma), from bile ducts, an adenoma (benign cholangioma) and carcinoma (malignant

parts of the world, being greatest in orientals and smallest in northern European Russia. It occurs at all ages from infancy to senility with a preponderance in the fifth decade, and it affects males twice as frequently as females. *Symptoms and signs* consist of: swelling of the abdomen, pain in the epigastrium or right upper quadrant of the abdomen, hematemesis, dyspepsia, anorexia, loss of weight, edema of the legs, jaundice, nausea and vomiting, weakness, ascites (due to portal hypertension and hypoproteinemia), anemia of the primary or secondary type, hepatomegaly, splenomegaly, hemorrhoids, fever and evidence of collateral circulation as enlargement of veins around the umbilicus and esophageal narices. The *causes of death* are liver insufficiency (cholemia), esophageal hemorrhage, secondary infection and superimposed hepatic car-

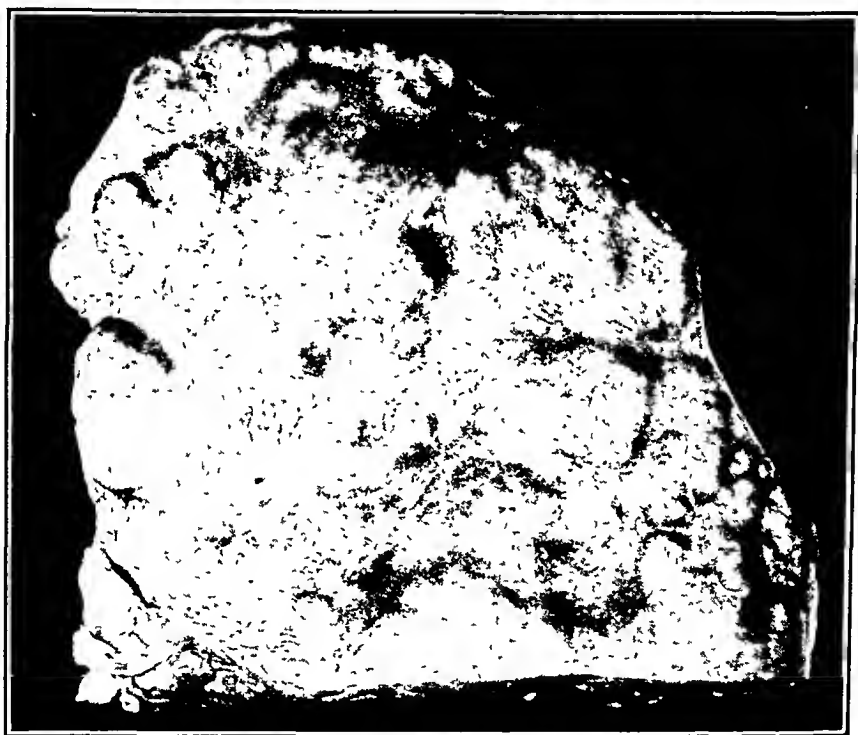


FIG. 314.—Portal cirrhosis of the liver.

cinoma. There are three essential types of cirrhosis—portal, pigmentary and biliary.

Portal cirrhosis is also known as atrophic cirrhosis and Laennec's cirrhosis. In the past numerous theories have been promulgated to explain its *cause*, but it was not until the last decade that real progress has been made. At the present time, it seems clearly established that dietary deficiency and particularly avitaminosis B is the most important etiological agent. Alcohol is doubtlessly a factor, but it works by way of an inadequate diet and not directly. In one-half the cases, the *liver* is reduced in size but in others, it is normal or increased to 3000 gm. Externally, the surface is finely or coarsely granular or more frequently nodular (Fig. 314). The nodules measure less than a millimeter or many centimeters in diameter and are uniform or irregular. Between them there are

gestion, cholangitis and hepatolithiasis. It occurs at all ages from infancy to senility, but is most common in the sixth decade, it affects males three times as frequently as females, and it predominates in orientals, Caucasians and African Negroes. *Symptoms and signs* are loss of weight, jaundice, mild or severe hepatic or epigastric pain, vomiting, fever, swelling of the abdomen and ankles, anemia, palpable nodular tumor in the region of the liver, ascites, failure to visualize the gallbladder by means of radio-opaque dye concentration studies, and downward displacement of the upper gastro-intestinal tract by an extraluminal mass. The *diagnosis* is established by laparotomy, peritoneoscopy (with biopsy) and needle aspiration through the abdominal wall. Secondary carcinoma of the liver, which is much more frequent, offers the greatest difficulty

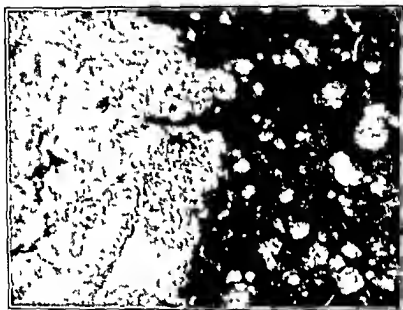


FIG 315 —Primary carcinoma of the liver disclosing a large mass and satellite nodules

in differentiation. Pathologically, primary carcinoma of the liver is of two types—liver cell or bile duct with sometimes combinations of both.

Liver cell carcinoma (malignant hepatoma) is more common than the bile duct variety. Cirrhosis may be primary and severe, slight and secondary, or there may be none whatsoever. Grossly, the lesion may be solitary or multiple. Solitary growths are sharply circumscribed, bulky, yellowish brown, solid and soft and measure as much as 20 cm in diameter (Fig 315). They tend to undergo softening, necrosis, hemorrhage and rupture. Multiple growths produce a more or less diffuse enlargement of the liver. The nodules are similar in appearance to the solitary tumor with the exception that they are smaller. Sometimes they are so small and so uniform that they are indistinguishable from regenerating lobules in portal cirrhosis. Usually, however, there are some nodules that can be

cholangioma); from blood vessels, a hemangioma, hemangioendothelioma and hemangiosarcoma; from lymphatics, a lymphangioma; from connective tissue, a fibroma and fibrosarcoma; from mesodermal, ectodermal and entodermal elements, a teratoma; from lymphoid tissue (reticulum cells), a lymphoblastoma, and from distant areas, metastatic melanblastoma, carcinoma and sarcoma. The four most important groups of tumors are hemangioma, adenoma, primary carcinoma and metastatic neoplasms.

Hemangioma.—This tumor is more common in the liver than in any other internal organ. Usually, the *lesions* are incidental findings at necropsy and of no clinical significance. Sometimes, however, they become large enough to produce symptoms. The smaller tumors are single or multiple, usually situated beneath the capsule, depressed, red or purple, spongy and measure less than 2 cm. in diameter. *Histologically*, they are usually of the cavernous type. Less frequently, they grow to 15 or 20 cm. in diameter, occupy a large portion of the liver or are pedunculated, become adherent to and displace adjacent organs, and may be complicated by hemorrhage. These larger growths are discovered at all ages from childhood to senility but most often in the fifth decade, and affect females five times as frequently as males. *Symptoms and signs* consist of a mass in the epigastrium, enlargement of the abdomen, pain, nausea, vomiting and anorexia. Small and asymptomatic lesions are left alone whereas larger, bulky and clinically bothersome growths are surgically resected. A *malignant transformation* of a cavernous hemangioma rarely if ever occurs, but it must be remembered that, albeit infrequently, some of these tumors are malignant (hemangioendothelioma and hemangiosarcoma) from the start. The *prognosis*, in general, is good.

Adenoma.—Adenoma of the liver is of the *hepatic* or bile duct type. Clinically, the former is more important. It occurs as sharply circumscribed, well-encapsulated, light brown, grey or yellowish, moderately firm solid nodules that measure as much as 15 cm. in diameter. *Histologically*, it is composed of cords nests or alveoli of large polyhedral cells with abundant acidophilic cytoplasm that resemble the structure of the liver. Sometimes the cells are more irregular and transitions to frank carcinoma are not uncommon. Since one can not be certain grossly that the neoplasm is not already cancer and since it tends to become malignant, *treatment* is excision. Adenomas of *bile ducts* rarely measure more than 3 cm. in diameter. They appear as greyish white encapsulated nodules and are frequently located just beneath the surface. *Histologically*, they are composed of acini lined with cuboidal or columnar cells. The cytoplasm is clear and the nuclei are round or oval and evenly stained. These tumors are innocent and usually produce no clinical disturbances.

Primary Carcinoma.—Primary carcinoma of the liver is said to occur from 0.13 to 0.66 per cent of all necropsies. Its precise *cause* is unknown but the following are considered of etiological significance: cirrhosis in about 75 per cent of cases, parasitic infection (schistosomiasis), syphilis, congenital re e con-

cells are not encountered. The stroma in bile duct carcinoma, unlike that in the liver cell type, is always abundant, dense and fibrous. Distinct metastasis is infrequent. There is no satisfactory treatment. Death occurs in 100 per cent of cases.

Metastatic Neoplasms—*Secondary tumors* of the liver are twenty times as common as primary growths. The source is more often carcinoma of the stomach, colon, esophagus and pancreas and less often breast and lung. Mention should also be made of melanoblastoma of the liver which is probably always secondary to a primary focus elsewhere, especially the eye. The route of involvement is by blood stream, lymphatics and less often by direct extension. The lesions are usually multiple, have no particular predisposition for any site and measure from a few millimeters to 15 to 20 cm in diameter. As a rule, they are sharply circumscribed, externally



FIG. 317—Bile duct carcinoma of the liver disclosing an abundant fibrous stroma that contains small acini and irregular groups of cells. $\times 100$

umbilicated, greyish white, firm and on section are homogeneous or, when larger, disclose central areas of necrosis and hemorrhage. Signs and symptoms are similar to those of primary carcinoma, for which they are mistaken in about one-half of the cases. There is, of course, no effective treatment. In lesions of the large bowel with metastasis to the liver, however, patients have been known to live for as many as five years after laparotomy in comparative comfort.

Mechanical Disturbances—In the liver, mechanical disturbances consist of jaundice (considered in connection with the bile ducts), hepatolithiasis, trauma and portal hypertension. Trauma may be encountered during manipulation at the time of surgery, following a blow to the abdomen, or consequent to a penetrating injury such as stab wound or gun shot wound. The latter are serious for they are usually associated with profound shock and hemorrhage. The mortality rate is high.

definitely identified as tumor. *Histologically*, the cells, as a rule, have some semblance to hepatic cells (Fig. 316). They are arranged in diffuse sheets; cords, nests or alveoli. They vary in shape and size but are generally polyhedral and larger than normal cells. Sometimes they assume gigantic proportions. The cytoplasm is homogeneously acidophilic until the tumor becomes highly undifferentiated when it is slightly basophilic. The nuclei are irregular, large, hyperchromatic, and in the larger cells are often multiple. The stroma in the tumor proper is scanty and composed mostly of capillaries. When present the accompanying cirrhosis is of the ordinary type. *Spread* of liver cell carcinoma is usually intrahepatic but it sometimes does extend to the hilar lymph nodes, lungs, bones and elsewhere. The solitary type is particularly prone to remain localized and can, therefore, be *treated* by surgical extirpation.

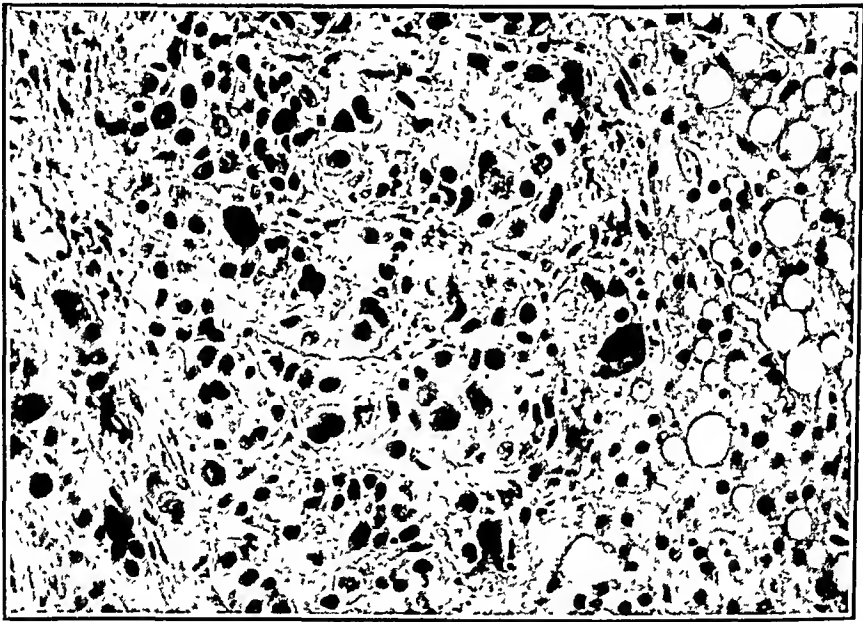


FIG. 316.—Liver cell carcinoma showing large eosinophilic cells with hyperchromatic nuclei arranged in small nests and cords. To the right there are a few normal cells present for contrast. $\times 100$

Reports of such treatment indicate 40 per cent three to seven year survival. There is no satisfactory treatment for the multiple variety and the *prognosis* is, therefore, universally poor.

Bile duct carcinoma are practically always associated with advanced cirrhosis. The *liver* is, therefore, diffusely enlarged and routinely greenish yellow. As a rule, the neoplasm affects the whole organ in the form of innumerable finely pebbled discrete or confluent nodules and less often as larger masses. One characteristic feature is the extreme uniform hardness of the entire liver. *Histologically*, most of the tumors are adenocarcinoma with varying degrees of anaplasia. The acini are grouped in clusters or permeate between the liver cords (Fig. 317). The cells are cuboidal, columnar or irregular and have a moderate amount of clear cytoplasm and round or oval uniform vesicular nuclei. Mitoses are frequent but giant

the liver by connective tissue. The gallbladder consists of (1) the fundus or blind end which is directed down, forward and to the right beyond the free edge of the liver to contact the anterior abdominal wall, (2) the body which is the intermediate part that lies between the liver above and the transverse colon below and (3) the neck which connects the body with the cystic duct. The mucosa of the *cystic duct* is thrown into about a dozen spiral folds that act as valves. The *common bile duct* courses downward anterior to the epiploic foramen, behind the first portion of the duodenum, between the pancreas and the left side of the second portion of the duodenum, and unites with the pancreatic duct to form the *apulla of Vater*. The latter empties into the second portion of the duodenum at the *duodenal papilla*, and in its distal portion contains the sphincter of Oddi. The *arterial supply* to the liver accompanies the bile ducts. The common hepatic artery ordinarily arises from the celiac artery and divides into a right and a left hepatic artery which enter the respective lobes of the liver. The gallbladder is supplied by the cystic artery which normally arises from the right hepatic, receives its *nerius* from the sympathetics and left vagus, and is drained by *lymphatics* which empty through the liver hilar nodes into those along the inferior vena cava.

Histologically, the gallbladder and bile ducts are essentially similar. They are composed of (1) a mucosa of tall columnar epithelium with oval basilar nuclei, (2) a lamina propria of connective tissue and elastic fibers which contains scattered lymphocytes and leukocytes, (3) a layer of smooth muscle the fibers of which run in several directions and (4) a serosa composed of an outer layer of mesothelial cells and an inner layer of collagenous connective tissue that contains blood vessels, nerves and lymphatics.

PATHOLOGY

Congenital Anomalies—Developmental abnormalities of the extrahepatic biliary system are numerous but usually trivial enough to be accordant with normal life. They may be listed as follows: (1) *gallbladder*—absent, double, bifid, inferior to left lobe of liver, retrodisplaced, in gastrohepatic ligament, within liver, attached to liver by mesentery (floating), transverse, subcutaneous and giving rise to a diverticulum (2) *bile ducts*—(a) common bile duct—cystic dilatation, absent and atresia, (b) cystic duct—parallel to common bile duct for 3 to 4 cm. before it joins, spiral to empty into the common duct on the left side, double, absent, and emptying into an accessory right hepatic duct, (c) common hepatic duct—absent and (d) right hepatic duct—accessory duct which joins the gallbladder, cystic duct, right hepatic duct or common hepatic duct and (3) *arteries*—(a) common hepatic—from abdominal aorta or superior mesenteric artery and absent in which case the main branches emerge directly from the celiac artery (b) right hepatic—from superior mesenteric or abdominal aorta and accessory right hepatic artery arising from left hepatic, aorta, superior mesenteric or gastroduodenal and (c) cystic artery—from the left hepatic or

Portal hypertension may be defined as an increase of pressure in the portal vein and its tributaries, consequent to some form of *block* to the flow of blood. The latter occurs (1) *intrahepatically*, examples of which are cirrhosis and Cruveilhier-Baumgarten disease and (2) *extrahepatically*, from thrombosis of the portal vein or one of its main tributaries due to infection, neoplasm or trauma. In children, a cause of extrahepatic occlusion is an extension into the left portal vein of the obliterative process which normally occurs at birth in the umbilical vein and ductus venosus. Portal block is *manifested* by secondary anemia, leukopenia, thrombocytopenia, splenomegaly, repeated gastric hemorrhages from esophageal varices and frequently ascites. It is in effect *Banti's syndrome*. *Esophageal varices* result from an attempt to establish a collateral circulation. Other communications between the portal and systemic veins are: from the colon and duodenum into the left renal vein, from the liver by way of the falciform ligament into the epigastric, internal mammary and ozygos veins, from the intestine into the inferior vena cava, from the rectum by the middle and inferior hemorrhoidal veins uniting with the superior hemorrhoidal, and from the portal vein to the inferior vena cava by a patent ductus venosus. In an effort (1) to decrease the portal pressure, (2) to rid of the esophageal varices and (3) to deal with ascites, the following *respective operations* have at one time or another been advocated (1) splenectomy, omentopexy and shunting of the portal into vena caval circulation by anastomosing the splenic to the left renal vein or the portal vein to the inferior vena cava, (2) ligate tributaries to the esophageal venous plexus or inject esophageal varices with sclerosing solutions and (3) suturing a renal pelvis to peritoneum, the saphenous vein to the peritoneum and the peritoneum to the subcutaneous tissue. The only one of these procedures that offers promise is the portacaval anastomosis.

BILIARY SYSTEM

EMBRYOLOGY

The development of the extrabiliary tracts has been considered under embryology of the liver.

ANATOMY

From the porta hepatis of the liver the extrahepatic biliary system emerges as the right and left *hepatic ducts*. These unite to form the common hepatic duct which measures from 2.5 to 4 cm. in length. The cystic duct coming from the gallbladder measures from 1.5 to 3.5 cm. in length. It unites at an acute angle with the common hepatic duct to form the common bile duct (ductus choledochus) which measures from 5.0 to 9.5 cm. in length and empties into the duodenum. The *gallbladder* is conical in shape, measures 7 to 10 cm. in length and 3 cm. in greatest width, and has a capacity of from 30 to 50 cc. Its superior surface is attached to the under surface of

the liver by connective tissue. The gallbladder consists of (1) the fundus or blind end which is directed down, forward and to the right beyond the free edge of the liver to contact the anterior abdominal wall, (2) the body which is the intermediate part that lies between the liver above and the transverse colon below and (3) the neck which connects the body with the cystic duct. The mucosa of the *cystic duct* is thrown into about a dozen spiral folds that act as valves. The *common bile duct* courses downward anterior to the epiploic foramen, behind the first portion of the duodenum, between the pancreas and the left side of the second portion of the duodenum, and unites with the pancreatic duct to form the *apulla of Vater*. The latter empties into the second portion of the duodenum at the duodenal papilla, and in its distal portion contains the *sphincter of Oddi*. The *arterial supply* to the liver accompanies the bile ducts. The common hepatic artery ordinarily arises from the celiac artery and divides into a right and a left hepatic artery which enter the respective lobes of the liver. The gallbladder is supplied by the cystic artery which normally arises from the right hepatic, receives its *nerves* from the sympathetics and left vagus, and is drained by *lymphatics* which empty through the liver hilar nodes into those along the inferior vena cava.

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gastroduodenal and accessory cystic from the common hepatic or left hepatic. Of the aforementioned group of anomalies, only two will be briefly considered—diverticula of the gallbladder and congenital cystic dilatation of the common bile duct.

Diverticula of the Gallbladder.—These may be *congenital* or *acquired*. The former are rare. They are of varying shapes (usually globular) and sizes, communicate with the gallbladder by a large or small ostium, and contain all the coats of this organ. *Acquired diverticula* on the other hand are found in about 15 per cent of normal and 90 per cent of infected gallbladders. They have also been *called* Luschka's crypts, Rokitansky-Aschoff sinuses, adenoma of the gallbladder, cholecystitis glandularis, cholecystitis cystica, cholesterol cysts, fibroadenoma, cystadenoma and pre-cancerous proliferations. They are *microscopic*, direct or tortuous

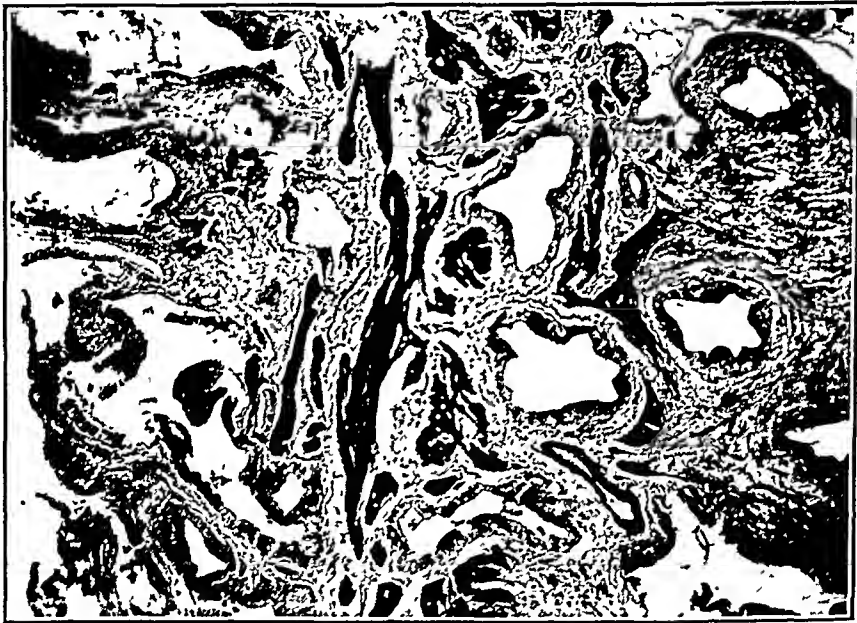


FIG. 318.—Diverticula in a chronically infected gallbladder. Note the marked fibrosis of the serosa and penetration of glands through the entire wall x 37 5.

sinus tracts of the mucosa that herniate through various layers of the wall and often come to lie beneath the mesothelium (Fig. 318). The anatomic basis for their origin is the lack of a submucosa, and the precipitating factor is an increase of intraluminal pressure resulting from a neurogenic dysfunction. The sinuses may be interrupted proximally, and the distal end become cystically dilated; they may become infected and form abscesses, and because of stagnation of bile they may become filled with calculi. From the histologic viewpoint, diverticula are important because the unwary may mistake them for carcinoma.

Congenital Cystic Dilatation of the Common Bile Duct.—This has also been *called* choledochus cyst, cystic dilatation of the common bile duct, choledochoceles, diverticulum and megalochodochus. It is said to occur once in 17,381 operations on the biliary tract, is more common in Japanese people, is usually manifest before twenty-

five years of age and is found in females in over three-quarters of the cases. Although numerous theories have been promulgated to explain its *genesis*, the most attractive is that which holds an excessive proliferation followed by an excessive recanalization of epithelial cells during the respective stages of development of the common bile duct. *Symptoms* start in childhood and when the lesion is fully developed the diagnostic triad consists of tumor, pain and jaundice. *Grossly*, the dilatation is spherical, eccentric, and has a capacity of as much as 8 liters. Inferiorly, the dilatation starts above the duodenum and superiorly, it ends at the cystic and common hepatic ducts, but sometimes it also involves the cystic and right and left hepatic ducts. The wall measures 2 to 7.5 mm in thickness, the inner surface is rough and covered with deposits of bile, and the contents are thick and viscid or colorless, white and watery. *Histologically*, the lining may consist of scattered flat epithelial cells and the wall is fibrotic but may disclose remnants of the muscle layer. If untreated, the natural course of the disorder is death from biliary cirrhosis, cholangitis, hemorrhage or rupture. The treatment of choice is anastomosis of the cyst to the duodenum. In such cases, the mortality should not exceed 27 per cent.

Inflammations—The only important inflammatory lesion of the gallbladder is a non-specific infection which is commonly known as *cholecystitis*. The disease may be divided into acute and chronic stages, but since the two are closely associated and have many factors in common it is convenient to consider them together. As an abdominal disease, cholecystitis is exceeded in frequency only by appendicitis. It has been estimated that it occurs in 15 per cent of the population in the United States and in two-thirds of all cases coming to necropsy. The chronic form of the disease arises consequent to a severe attack or more commonly to repeated clinical or subclinical attacks of acute cholecystitis. Whereas formerly the latter was thought to be caused by bacteria, it is now known that chemicals are responsible for the initial changes and that bacteria, albeit frequently extremely important, are secondary invaders. Arguments advanced against bacteria being the precipitating factors are: cholecystitis is rare in children, while infection is common, it is infrequent in patients with gastrointestinal ulceration in whom the portal circulation is readily accessible to bacteria, cultures from two-thirds of cases of cholecystitis yield the same bacteria as do those from normal gallbladders, the histologic changes are different than those of ordinary bacterial infections, and at operation the abdominal wound almost always heals by first intention. The chemical agents responsible for the inflammation are bile and its salts and pancreatic juice. Evidence for this is mostly experimental, but is unequivocal. In animals acute cholecystitis identical with that in man has been produced (1) by ligating the cystic duct with or without the injection of concentrated bile, but if the duct is ligated and the bile is removed no inflammation develops, (2) by injecting bile or bile salts into the cystic duct, (3) by injecting bile or bile salts into the portal vein when the cystic duct is patent, but not when it is ligated and (4) by injecting the common bile duct

gastroduodenal and accessory cystic from the common hepatic or left hepatic. Of the aforementioned group of anomalies, only two will be briefly considered—diverticula of the gallbladder and congenital cystic dilatation of the common bile duct.

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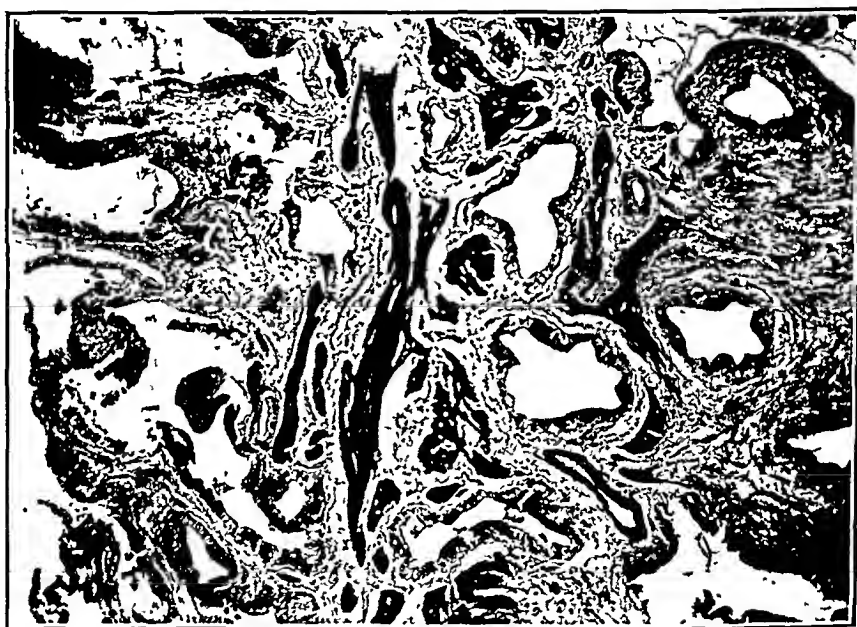


FIG. 318—Diverticula in a chronically infected gallbladder. Note the marked fibrosis of the serosa and penetration of glands through the entire wall x 37.5.

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and contains adherent masses of grey precipitate, and the lumen often contains stones and thick bile or purulent material (Fig 319). In more advanced cases the wall becomes blackened (gangrenous), thinned and may perforate or the lumen becomes greatly distended with pus (*empyema* of the gallbladder). Perforation may occur into the peritoneal cavity and result in peritonitis, into surrounding adhesions to produce an abscess or into the liver also to form an abscess. More frequently, however, the process completely resolves or leaves only a slight residuum. After repeated acute attacks and partial resolutions or as a result of a continued smouldering infection, the gallbladder passes into the chronic stage of infection. Such an organ is enlarged or contracted and distorted. The serosa is opaque, thick, tough and fibrous and often contains adhesions, the wall is, as a rule, greatly thickened, rigid and firm, the mucosa may appear grey and eroded, and the lumen is frequently contracted



FIG 320 — Chronic cholecystitis and cholelithiasis. The gallbladder is contracted and the wall is thick and fibrotic.

and is filled with stones or with clear colorless watery fluid (Fig 320). *Histologically*, the earliest changes consist of congestion of the vessels, intense edema most marked in the serosa, focal extravasation of erythrocytes, and a sprinkling of neutrophils, monocytes and plasma cells. When bacteria are added the picture changes to one of suppuration. This exists as a severe infiltration of neutrophils (sometimes with the formation of abscesses), an outpouring of fibrin and a proliferation of fibroblasts. The mucosa is usually involved in this process, becomes necrotic and sloughs. As the infection subsides eosinophils appear in great numbers (subacute cholecystitis) and if the infection smoulders, these become replaced with monocytes, plasma cells and lymphocytes to constitute the active phase of chronic cholecystitis. In time, even these cells disappear and the residuum consists of a mass of fibrous tissue. This may be minimal or it may be so extensive that none of the normal constituents of the wall is recognizable. In addition to the fibrosis, some of the gallbladders acquire calcium phosphate and less commonly calcium oxalate to become partly or completely calcified.

A diagnosis of cholecystitis is established from a history of symptoms already listed, particularly when they are present in a woman

with pancreatic juice. In man, evidence that pancreatic juice is of etiological significance is indicated by the fact that high concentrations of amylase and lipase have been reported in the contents of acutely inflamed gallbladders. With regards to bile as a causative agent, however, there is only the fact that almost all cases of acute cholecystitis reveal partial or complete occlusion of the cystic duct. In over 90 per cent of the cases, this is caused by calculi while in the rest it is due to previous inflammation or congenital narrowing of the lumen. Once chemical inflammation has been initiated, bacteria (which normally and intermittently inhabit the gallbladder or which abnormally are carried there by the blood stream) secondarily invade the wall and produce an ordinary suppurative type of lesion.

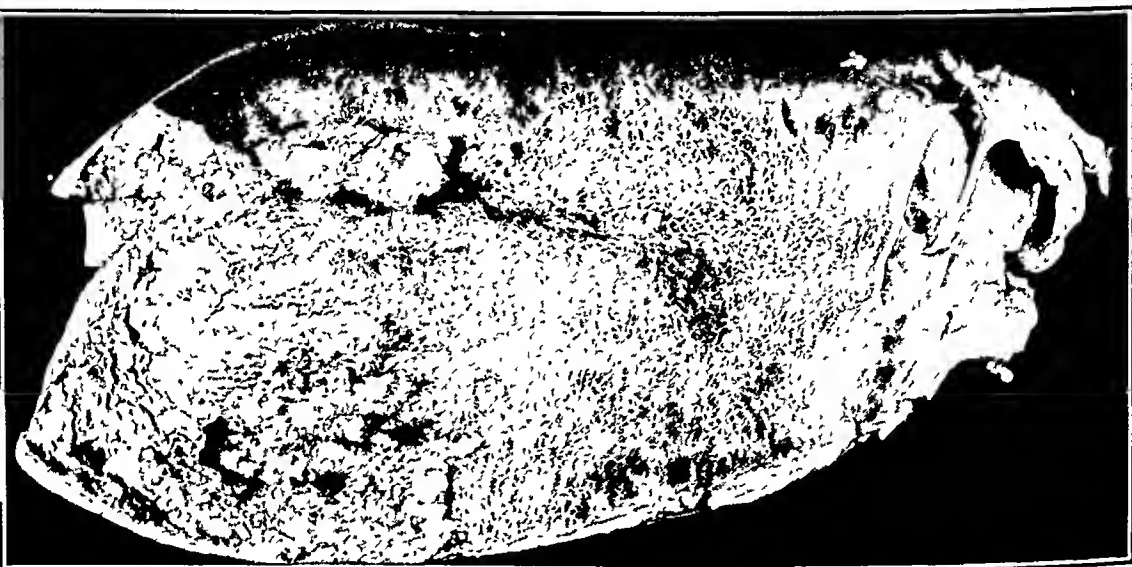


FIG 319.—Acute cholecystitis The mucosa is covered with an exudate.

Cholecystitis affects women four times as frequently as it does men and usually occurs beyond the age of thirty-five years with a peak in the early part of the sixth decade. Acute attacks, as a rule, succeed *chronic cholecystitis*, which is manifested by vague indigestion, epigastric discomfort, belching, nausea and vomiting, inability to eat greasy foods, loss of weight and jaundice. These symptoms are often present intermittently for twenty or thirty years. A superimposed *acute inflammation* is evidenced by: pain in the epigastrium or right upper quadrant that radiates to the back, right shoulder or across the abdomen, colic, nausea, vomiting, chills, fever, jaundice, weakness, tenderness in the right upper quadrant, abdominal rigidity, a palpable mass in the region of the gallbladder and leukocytosis. Cholecystography may show calculi and in chronic infections, dye excretion tests will often reveal a non-functioning gallbladder.

Grossly, acutely inflamed gallbladders are usually enlarged; the serosa is dull, dry, may be covered with a fibrinous or fibrino-purulent exudate and on sections drips edema fluid; the wall is thick, firm and rigid; the mucosa is irregularly congested ulcerated

mately sixty per cent of the cases there is a history of previous gall-bladder disease, the average duration of which is about twelve years. This exists in the form of intermittent colic, indigestion, epigastric discomfort and intolerance to fatty food. When cancer develops there is usually a *change in symptoms*. In decreasing order of frequency, the recent episode is manifested by pain, loss of weight, dyspepsia, weakness, anorexia, jaundice, constipation and vomiting.

Grossly, the gallbladder may be normal in size, enlarged or contracted. The wall, as a rule, shows evidence of chronic cholecystitis and is such is thick, rigid, grey and fibrous. The lumen may be of normal size, dilated or decreased, it usually contains stones, and it



FIG. 322.—Carcinoma of the gallbladder. $\times 37.5$

may be filled with thick or thin bile or pus. The cancer involves the fundus in over one-half of the cases, the mid portion in over a quarter and the neck in the remainder. More often it exists as an infiltrating type of growth wherein the involved wall is thicker than its adjacent portion, extremely firm, occasionally friable but ordinarily elastic, grey with sometimes scattered irregular yellow foci and indefinitely defined so that it is impossible to say where the tumor stops (Fig. 321). Such growths ordinarily affect only a portion of the organ but because of the accompanying fibrosis they produce considerable distortion. Less commonly, the tumor is a fungating, fissured, friable, pink, brown or bile stained mass that projects into the lumen and is attached to the wall by a broad pedicle. *Histologically*, 98 per cent of the growths are glandular and 2 per cent are squamous. The former appear as well-differ-

beyond the age of forty-five years. Cholecystography is of indispensable value. In chronic infections, *treatment* should be cholecystectomy for such patients are subject to repeated acute attacks and what is even more important they may, in the presence of stones, ultimately develop carcinoma. Treatment of acute cholecystitis is less standardized, although within the last decade most surgeons resort to immediate cholecystectomy if the patient can stand the procedure or to cholecystostomy if his physical condition is poor. The post operative *mortality* should not exceed 6 per cent. The causes of *death* in these cases are usually pneumonia, cardiac failure and diabetes.

Tumors.—Classified histogenetically, the following tumors have been described as arising in the *gallbladder*: from epithelium, an adenoma, papilloma and carcinoma; from connective tissue, a fibroma, fibrosarcoma, myxoma and myxosarcoma; from fat, a



FIG 321 —Carcinoma of the body of the gallbladder

lipoma; from muscles, a myoma and myosarcoma, and from vessels, an angiosarcoma and endothelioma. Tumors of the extrahepatic *bile ducts* are less protean and consist of: from epithelium, an adenoma, papilloma and carcinoma; from connective tissue, a fibroma; from muscle, a myoma; from nerve tissue, a neuroma, and from distant areas, metastatic tumors. The only two tumors that will be considered further are carcinoma of the gallbladder and carcinoma of the extrahepatic bile ducts.

Carcinoma of the Gallbladder.—This is said to constitute from 2.8 to 6 per cent of all cancers found at necropsy and less than 1 per cent of all operations on the biliary tract. It affects females four times as frequently as males, and has been recorded in patients from twenty-eight to eighty-five years of age with the majority in the sixth decade. The *cause* as in other cancers is not known, but since calculi are found in as many as ninety-four per cent of the cases, it is thought that chronic irritation plays a dominant rôle. In approxi-

frequently than traumatic rupture of the liver or bile ducts. It results from kicks, falls, blows or crushing injuries and when the trauma is non-penetrating, it can occur only when the organ is distended with bile. There is, of course, extravasation of bile into the peritoneal cavity, and the acute symptoms that develop are those of bile peritonitis. Treatment consists of suturing the defect.

Cholelithiasis—Gallstones are found in about one-third of all cases coming to necropsy. They are more frequent in women than in men and are usually found in patients beyond the age of forty years. Aside from bouts of colic wherein there is severe epigastric or right upper abdominal pain that radiates to the back or right scapula, symptoms and signs are those of cholecystitis. In about one half of all cases, however, gallstones are without any manifestations. There are three types of calculi—pigment, cholesterol and mixed. *Pigment stones* are metabolic in origin and result from a precipitation of biliverdin and bilirubin from a supersaturated solution of bile. They may be found in the intrahepatic or extra-



FIG. 323—Cholesterosis of the gallbladder

hepatic bile ducts or the gallbladder. Initially, they exist as small, irregular or elongated, friable or soft putty-like masses of dark green, black or dark brown material, but if they are found in the gallbladder, they may become coated with cholesterol. These stones are found in cases in which there is an extensive destruction of blood. *Cholesterol stones* were at one time considered as being metabolic in origin but are now known to arise on an infective basis. Their genesis is as follows. Inflammation of the gallbladder results in an excess secretion, by the mucosa, of mucin and cholesterol. The mucin along with clumps of bacteria and epithelial cells forms a nucleus around which the amorphous cholesterol is deposited by a process of adsorption. Crystallization of the cholesterol occurs as a secondary process. Cholesterol stones are usually single but may be several in number. They are oval, nodular, light yellow and measure 3 to 4 cm. in diameter. On section the outer layers are amorphous, while the center contains radiating crystals. *Mixed stones* are composed of bilirubin, cholesterol and calcium and also develop on an infective basis. They may be single, several or

entiated acini or as more anaplastic masses of usually cuboidal or columnar cells with basilar nuclei and relatively clear cytoplasm (Fig. 322). Sometimes they secrete an abundant amount of mucoid material, forming an appearance similar to mucinous carcinoma of the gastrointestinal tract. The tumor may affect only the mucosa but, generally, it penetrates throughout the wall. It is always accompanied by an inflammatory reaction. Cancer of the gallbladder *spreads* by extending to the liver, bile ducts, duodenum, colon and abdominal wall and by metastasizing to the liver, lymph nodes, pancreas, omentum, ovaries and other areas.

A correct *diagnosis* is seldom made clinically for the history is not distinctive. It should be suspected, however, if there is a change in symptoms suggesting chronic cholecystitis. The only effective *treatment* is surgical extirpation of the gallbladder. This can be accomplished in less than 25 per cent of the cases, for in the rest the disease at laparotomy is already too extensive. The *cure* rate is extremely low.

Carcinoma of the Extrahepatic Bile Ducts.—This is about as common as carcinoma of the gallbladder. It affects males about five times as frequently as females and has a peak incidence in the sixth decade. *Symptoms* are those of biliary obstruction, develop early in the course of the disease and in 90 per cent of cases appear acutely. They consist of jaundice, pain, pruritis, loss of weight and strength, vomiting, anorexia, fever, diarrhea or constipation, nausea, flatulence and belching. Except for being smaller, the growths both *grossly* and *microscopically* are similar to those in the gallbladder. In the approximate order of frequency the *locations* are: ampulla of Vater, common bile duct, junction of common bile hepatic and cystic ducts, common hepatic duct and cystic duct. *Spread* occurs by extension along the ducts and late in the course of the disease to the lymph nodes, liver and pancreas. Associated lesions in the biliary tract and liver are: cholangitis, abscess, cirrhosis, hydrops of the gallbladder and empyema of the gallbladder. The *treatment* of choice is excision with pancreaticoduodenectomy. The *prognosis* in the past with less radical operations has been poor, but with this procedure the future appears more optimistic.

Mechanical Disturbances.—Under this heading will be considered cholesterolosis of the gallbladder, traumatic rupture of the gallbladder, cholelithiasis, biliary fistulas and jaundice.

Cholesterolosis of the Gallbladder.—This has also been called lipoid or strawberry gallbladder. It is frequently associated with cholesterol stones and *grossly*, exhibits a diffuse yellow flecking of the summits of the mucosal folds (Fig. 323). *Histologically*, there is a deposition of cholesterol esters in the epithelial cells themselves and in distended histiocytes in the submucosa proper. The latter take on the appearance of ordinary foam cells. Although it is known that cholesterol is secreted by the epithelial cells of the gallbladder, the mechanism resulting in this condition is not known. The lesion is of no known practical significance.

Traumatic Rupture of the Gallbladder.—This occurs less frequently than does spontaneous rupture of this organ and also less

PANCREAS

EMBRYOLOGY

The pancreas is detectable in the 3 to 4 mm embryo as *two buds* arising from the duodenum—a *dorsal* one just proximal to the hepatic diverticulum which forms the dorsal pancreas, and a *ventral* one in the distal angle formed between the duodenum and the hepatic diverticulum which is known as the ventral pancreas. The dorsal pancreas grows into the dorsal mesentery, elongates and forms the neck, body and tail of the adult organ. The ventral pancreas, with its duct emptying into the common bile duct, is, by growth, carried to lie near the dorsal pancreas with which it fuses during the seventh week of embryonic life to form the head of the final pancreas. Its duct (Wirsung's) unites with that of the dorsal portion to form the main duct which thus empties into the common bile duct. The proximal segment of the duct of the dorsal pancreas (Santorini's) becomes accessory and empties directly into the duodenum. Both the islets of Langerhans and the acini first appear about the third month of embryonic life as terminal and side buds from the main ducts.

ANATOMY

The pancreas measures 12 to 15 cm in length, lies in the posterior portion of the epigastrium and left hypochondrium and consists

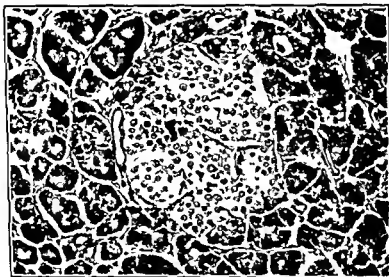


FIG. 324.—Normal pancreas x 100

from right to left of a *head, neck, body* and *tail*. The *head* lies within the loop of duodenum and is in intimate contact inferiorly with the superior mesenteric artery, laterally and to the right with the pancreaticoduodenal arteries, and posteriorly with the common bile duct. Other relations of the head and of the rest of the organ are

hundreds in number and measure from a few millimeters to 4 to 5 cm. in diameter. They are faceted smooth or nodular and grey, brown or black in color. Cut surface presents a laminated appearance with crystals centrally and amorphous material peripherally.

The *complications* caused by gallstones are: cholecystitis, pancreatitis (if impacted at the ampulla of Vater), cholangitis with intermittent jaundice, biliary fistulas, hydrops of the gallbladder (obstruction of the cystic duct and distention of the gallbladder with secretions), empyema of the gallbladder (an infected hydrops, or merely collection of pus within the lumen), obstruction of the ducts, and possible etiological rôle in the development of cancer.

Biliary Fistulas.—These may be divided into external and internal. *External fistulas* are those that drain through the skin. They usually follow a cholecystostomy or cholecystectomy and are formed because the resistance to passage of bile through normal channels is greater than that through the open wound or sinus tract. The *cause* is some obstruction and is commonly due to a stone, mucous plug, blood clot, débris or traumatic stricture. The material drained consists of mucus if the cystic duct is occluded or bile if the common bile duct is blocked. *Internal fistulas* occur between the gallbladder and duodenum, stomach, transverse colon, pelvis of the right kidney and peritoneal cavity. Ninety per cent are due to erosions by biliary calculi and the rest are *caused* by perforated peptic ulcer, carcinomas and trauma. *Treatment* of biliary fistulas is restoration of the flow of bile and secretions through natural channels. The procedure will depend upon the cause and type of fistula. The operative *mortality* rate is about 25 per cent.

Jaundice.—It may be defined as a yellowish discoloration of the skin due to bilirubin. Its *causes* are three (1) *prehepatic*—due to excess destruction of erythrocytes as seen in hemolytic jaundice, (2) *intrahepatic*—due to toxicity, infection or destruction of hepatic cells and (3) *posthepatic*—due to obstruction to the flow of bile through the biliary passages. The latter, and particularly when it affects the extrahepatic bile ducts, is of particular importance to the surgeon. To produce jaundice, the occlusion must obviously be in the hepatic or common bile ducts. Its *causes* may be enumerated as follows: (1) Congenital—stenosis, atresia, complete absence or congenital cystic dilatation of the common bile duct. (2) Inflammations—cholangitis and pancreatitis. (3) Neoplastic—primary benign or malignant tumors of the ampulla of Vater and bile ducts and secondary tumors. These may operate by causing compression from the outside such as carcinoma of the pancreas, duodenum or metastasis to regional lymph nodes, by diffusely permeating the walls of the ducts or by occluding the lumen by papillary implants in the mucosa. (4) Mechanical disturbances. These are due to foreign bodies, such as gallstones or ascaris lumbricoides or to benign strictures. Over 80 per cent of the latter are due to operative trauma, such as the result of excision, ligating, incision or accidental clamping of the common hepatic or bile ducts, or the result of ligating the cystic duct too closely to the confluence of the ducts.

fibromatosis of the pancreas, agenesis of the exocrine portion of the pancreas, cirrhosis of the pancreas, polycystic pancreas and congenital familial steatorrhea. It is said to occur in 3.5 per cent of all children coming to necropsy and is thought to result from (1) segmentation and resorption of the pancreatic duct and its branches followed by cystic dilation of the remnants and atrophy of the acini, (2) congenital atresia or stenosis of the pancreatic ducts and bronchi, (3) obstruction of pancreatic ducts from altered and inspissated secretions, (4) vitamin A deficiency and (5) viral infection. *Symptoms* develop in infancy and may be referred to the lungs in the form of chronic cough or frequent colds, or to the gastrointestinal tract manifested by failure to gain, foul greasy loose stools, emaciation and protruberant abdomen. Roentgenograms of the small intestine show delayed motility and altered mucosal pattern, and of the lungs, emphysema, atelectasis, pneumonia and bronchiectasis.

Grossly, the pancreas may be normal or decreased in size, lobulated and firm. Cut surfaces are grey, nodular and may disclose foci of calcification. The larger ducts are usually patent and less often occluded or absent. *Histologically*, they are dilated, tortuous and cystic. They are lined with flat and, rarely, with squamous epithelium and are filled with laminated eosinophilic secretions. The acini are also dilated, distorted, broken up and depleted, but the islets of Langerhans are usually normal. The interstitial tissue is greatly increased in amount, myxomatous or fibrotic and is infiltrated with lymphocytes and monocytes. The lungs both grossly and histologically show emphysema, atelectasis, pneumonia, abscesses and bronchiectasis.

A clinical *diagnosis* of fibrocystic disease of the pancreas is confirmed by demonstrating an absence or a decrease of pancreatic enzyme in duodenal contents. *Treatment* is medical and consists of bronchial aspirations or postural drainage, antibiotic and chemotherapy, high protein low fat diet and pancreatic extracts orally. The *prognosis* is guarded.

Solitary Cysts—These cysts of the pancreas are much more frequently acquired than they are congenital. They are all, however, included in this section for the sake of convenience. They are found at all ages, but predominate in the fifth decade of life and affect females more frequently than males. *Symptoms and signs* are pain in the epigastrium, nausea and vomiting, anorexia, constipation or diarrhea, jaundice and a palpable upper abdominal mass. Roentgenograms may disclose a silhouette of a cyst, and with the aid of barium an enlargement of the duodenal loop or displacement of the stomach and duodenal-jejunal flexure.

Pathologically, pancreatic cysts may be divided into the following five categories. (1) *Congenital*. These are developmental in origin and are sometimes associated with cysts of the liver and kidneys. They are single or multiple and, as a rule, unilocular, have smooth inner surfaces, are filled with pale yellow clear fluid that contains pancreatic enzymes, and measure as much as 8 to 10 cm. in diameter. The wall is thin. It is composed of connective tissue and is lined

(1) Posteriorly—inferior vena cava, right crus of diaphragm, aorta, left crus of diaphragm, left adrenal, left kidney, spleen and along the posterior surface of the body the splenic vein. (2) Anteriorly—transverse colon and mesocolon, coils jejunum, omental bursa and stomach. (3) Inferiorly duodenal-jejunal junction. (4) Superiorly—celiac axis. The *arterial* supply comes from the splenic hepatic and superior mesenteric vessels; the *veins* drain into the superior mesenteric and splenic vein; the *lymphatic* empty into adjacent nodes, and the *nerves* are derived from the vagus and splanchnic nerves.

Histologically, a loose connective tissue stroma contains vessels, nerves, Pacinian corpuscles, pancreatic ducts, acini and islets of Langerhans. The ducts are composed of a basement membrane lined with columnar cells. Between these are found scattered goblet and argentaffine cells. The terminal portion of the ducts are continuous with the acini. The latter form the external secretion of the pancreas and are composed of a single row of pyramidal cells that line a delicate reticular membrane (Fig. 234). The internal secretion of the pancreas (insulin) comes from the islets of Langerhans. They consist of sharply delineated clusters of syncytial-like cords of cells. Their cytoplasm is more abundant and lighter than that of the acini and, when specifically stained, it discloses alpha and beta granules.

PATHOLOGY

Congenital Anomalies.—Some developmental abnormalities of the pancreas are inconsequential whereas others are important. They may be listed as follows: (1) The *accessory duct* forms the main duct which thus opens directly into the duodenum. (2) *Absence* of the dorsal pancreas. (3) *Failure of union* of the two pancreases with persistence of both ducts. (4) *Accessory pancreases*. These usually occur in the wall of the stomach, duodenum and jejunum, but they have also been found in the ileum, Meckel's diverticulum, umbilical fistula, mesentery, omentum, spleen, gallbladder, cystic and common ducts, liver, transverse mesocolon and teratomas. They probably originate from inclusions of original pancreatic tissue within these organs when, at the time of early development, they lie in close proximity to the pancreas. They are important because they may cause hypoglycemia and because they may become the seat of benign and malignant tumors, cysts, inflammation, necrosis and hemorrhage. (5) *Annular pancreas* consisting of an encirclement of the second portion of the duodenum by an anterior and a posterior arm of the head of the pancreas. The result may be obstruction to the intestine, common bile duct or portal vein. Treatment consists of a division of the ring, gastroenterostomy or duodenojejunosomy. (6) *Fibrocystic* disease. (7) *Solitary cysts*. The latter two will be discussed in greater detail.

Fibrocystic Disease.—Fibrocystic disease of the pancreas has *also* been *called* congenital pancreatic disease, atrophy of the pancreas, congenital pancreatic steatorrhea, celiac disease, congenital cystic

are liberated and produce extensive destruction of the pancreatic tissue. Digestion of vessel walls causes hemorrhage, and the action of lipase on fat results in its necrosis with the formation of glycerine and fatty acids. The latter then unite with calcium to produce a soap. Clinically, there are sudden severe epigastric or upper abdominal pain, nausea, vomiting, cyanosis, shock, rigidity and tenderness of the abdominal muscles, abdominal distention, rapid pulse, leukocytosis and elevated serum amylase.

The pathologic changes depend upon the severity of the disease and the extent of damage. In milder and early cases, the gland is enlarged firm and edematous. There may or may not be associated areas of fat necrosis represented as small irregular chalky areas that are limited to the gland. In more severe cases, there is sanguineous fluid in the lesser peritoneal cavity and the pancreas is enlarged, soft, boggy and hemorrhagic. Fat necrosis is more extensive and involves not only the pancreas but also the omentum, mesenteric, extraperitoneal, diaphragmatic, mediastinal and pericardial deposits. In still more severe cases, the pancreas becomes partly or entirely digested, gangrenous and portions of it slough into the lesser peritoneal sac. At any time a leukocytic response may become overwhelming, so that there may be superimposed a frankly suppurative process with the formation of one or more abscesses. Histologically, in the early stages there are merely interstitial edema and a variable degree of neutrophilic infiltration. As the process becomes more severe, there are destruction and disruption of the normal parenchyma, massive necrosis and erythrocytic extravasation and an increase in neutrophils. Fibrosis becomes apparent when the necrosis and inflammation begin to subside. Fat necrosis has a characteristic microscopic appearance. The central area is composed of outlines of former fat cells that are partly or wholly filled with opaque amorphous eosinophilic material. At the periphery, due to the deposition of calcium, this material acquires a bluish tint. Beyond this, there is a zone of neutrophils, nuclear fragments and fibrin and this merges with a surrounding fibroblastic reaction.

Acute pancreatitis should be suspected in any case of upper abdominal pain. An elevated serum amylase confirms the diagnosis. Among others, a differential diagnosis includes coronary occlusion, acute cholecystitis, renal and biliary colic, perforated gastric or duodenal ulcer and acute appendicitis. Treatment of choice is conservative non-operative, but if the abdomen is opened the most that should be done is insertion of a drain to the capsule of the pancreas. The mortality in conservatively treated cases is about 5 per cent, whereas in surgically treated cases it is 33 per cent.

Chronic Pancreatitis—This results from low grade acute attacks that are separated by variable periods of complete inactivity and relative absence of clinical disturbances. Ultimately, however, the organ and especially the head is converted into a hard, irregular nodular mass that grossly is indistinguishable from carcinoma. Histologically, there is a progressive replacement of the pancreas by dense sclerotic fibrous tissue and a simultaneous disappearance of the acini and islets of Langerhans. There is, in addition, an

with a single layer of cuboidal or columnar epithelial cells. Occasionally, the inner surface may contain a few papillary excrescences. (2) *Papillary cystadenoma*. These are true tumors that grow in a papillary and cystic manner. They are uncommon, arise from the pancreatic epithelial cells, are circumscribed and round and usually measure 6 to 10 cm. in diameter. Externally they are bossed and smooth; the wall is of variable thickness but usually thin; its inner surface contains numerous papillae, and the lumen of the cyst is filled with milky or pale green fluid. Histologically, the wall and papillae are composed of connective tissue and are covered with cuboidal or columnar epithelial cells. Usually the cells are a single layer thick, sometimes they are heaped up to form several layers and in about 20 per cent of the cases they become irregular, invade the wall and are frankly cancerous. (3) *Retention*. These are multiple, seldom more than 1.5 cm. in diameter and eventuate from an occlusion of the ducts due to inflammation or stones. Retention cysts are of no clinical significance. (4) *Echinococcus* have already been described in the chapter on the peritoneum (p. 442). (5) *Pseudocysts*. These are by far the most common and represent the end result of acute pancreatitis or trauma to the pancreas. They originate in the vicinity of the pancreas and not within it. They are located within the lesser peritoneal sac and more specifically are found between the stomach and transverse colon, between the stomach and liver and under the gastrohepatic omentum, or between the layers of the transverse mesocolon. The initial step in their genesis is a hematoma. This becomes encapsulated and the blood, as a result of enzyme activity, is transformed into a milky fluid. Histologically, the wall is composed of fibrous tissue and is not lined with epithelium.

A *diagnosis* of pancreatic cyst is established from the history (especially pseudocysts), a palpable cystic swelling in the epigastrium and the characteristic roentgen changes already enumerated. *Treatment* is surgical removal or marsupialization. *Complications* in untreated cases consist of hemorrhage into the cyst, perforation into the peritoneal cavity or gastrointestinal tract, infection and diabetes (5 per cent of the cases). A cancerous transformation occurs in about 20 per cent of papillary cystadenoma. The operative *mortality* is less than 10 per cent.

Inflammations.—The only surgically important inflammatory lesions of the pancreas are non-specific acute and chronic pancreatitis.

Acute Pancreatitis.—This is *also called* acute hemorrhagic pancreatitis or acute pancreatic necrosis. Its *causes* are doubtlessly many and may be listed as (1) reflex of infected bile from the ampulla of Vater as a result of occlusion by a calculus or spasm of the sphincter of Oddi, (2) obstruction to outflow of pancreatic juice due to pancreatic calculus, to metaplasia of the ductal epithelium to a stratified squamous type or to inspissated secretions, (3) arterial spasm or occlusion, (4) bacteria that are carried to the pancreas from adjacent organs, or by way of the lymphatics and blood stream and (5) trauma. In any case, pancreatic enzymes

pyramidal cuboidal or irregular and deeper staining, and the lumens are small and empty or crowded. In more undifferentiated tumors the alveoli are distorted and only partly formed, and there are nests,

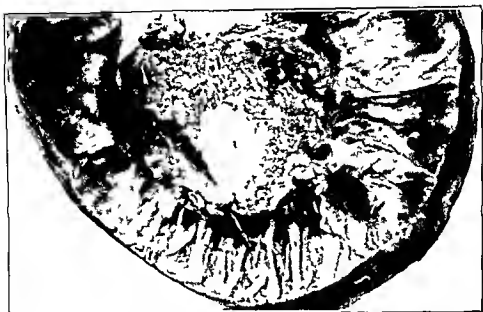


FIG. 325.—Carcinoma of the head of the pancreas removed surgically. An applicator is inserted in the common bile duct.



FIG. 326.—Adenocarcinoma of the pancreas. $\times 100$

ords, groups and single cells of varying shapes and sizes. The cytoplasm is abundant or scanty and vacuolated or solid. The nuclei are hyperchromatic and occasionally, several are present in a single cell. In the completely undifferentiated variety, the cells are oblong or spindle shaped, closely packed and resemble a sarcoma.

infiltration with varying numbers of plasma cells, lymphocytes, monocytes, eosinophils and giant cells. There may or may not be pseudocyst formation. The *cause* of the infection is not known. At first the only *symptom* is pain but later obstruction of the common bile duct results in jaundice, and destruction of the acini and islets of Langerhans produces digestive disturbances and diabetes. Surgical *treatment*, indicated in cases with jaundice, consists of re-establishing the flow of bile.

Tumors.—From a histogenetic point of view reported neoplasms of the pancreas consist of: from epithelial cells, tumors of the islets of Langerhans and carcinoma; from connective tissue, myxoma, fibroma and fibrosarcoma; from fat cells, lipoma; from lymphoid tissue (reticulum cells), lymphoblastoma, and from other organs and tissues, secondary tumors. *Secondary neoplasms* reach the pancreas by direct extension from neighboring organs, by way of the lymphatics and, from distant areas, by way of the blood stream. Although growths of the stomach, extrahepatic biliary tract and adjacent lymph nodes are the most frequent offenders, almost any organ or tissue in the body can be the site of the primary tumor. For all practical purposes the important neoplasms of the pancreas are two—carcinoma and islet cells tumors.

Carcinoma.—Carcinoma of the pancreas, unless otherwise specified, excludes cancer that reproduces the islets of Langerhans. It is said to comprise 1.3 to 2 per cent of all carcinomas, affects males twice as frequently as females and has a peak incidence in the sixth decade. *Symptoms and signs* are: upper abdominal pain, jaundice, loss of weight, constipation or diarrhea, nausea and vomiting, fever, anorexia, hematemesis, ascites, palpable epigastric mass and anemia. The pain, which may be severe particularly in cancer of the body and tail, is due to involvement of the nerves of the celiac plexus and the somatic sensory nerves of the posterior peritoneum. Jaundice in carcinoma of the head is caused by direct pressure on the common bile duct, and in carcinoma of the body and tail by metastasis to the liver. Ascites is caused by abdominal carcinomatosis and obstruction of the portal vein.

Two-thirds of carcinoma of the pancreas involve the head, while the rest are equally distributed through the remainder of the gland. The *tumor* is usually small so that there is little or no external disfiguration, although occasionally, it may be rather bulky (Fig. 325). Most of the tumors are ill-defined, grey to white, and stony hard. Less frequently, however, they are relatively soft and homogeneously grey with scattered yellow foci or are even mucoid in character. It is probable that all carcinomas arise from the ductal epithelium and that they then differentiate into structures that resemble ducts or acini or remain completely undifferentiated. Accordingly, *histologically*, there may be alveoli of cuboidal or columnar cells one or more layers thick that line a well-defined basement membrane (Fig. 326). The nuclei are round or oval, basilar and vesicular. The cytoplasm is densely eosinophilic, reticulated, vacuolated or mucinous and the lumen is empty or filled with granular or mucoid material. In others the alveoli are smaller; the lining cells are

somewhat reticulated cytoplasm, and round or oval uniformly and lightly staining vesicular nuclei. Less frequently, the cells are more irregular, the nuclei are pyknotic, they may be double or several may be piled up in a single cell, and mitoses may be present. Special stains reveal both alpha and beta granules. The stroma varies. It may be scanty, loose, and vascular, or abundant, dense, acellular and even partly calcified. While many of these tumors appear quite bizarre, even with invasion of the capsule, they are nevertheless clinically benign. There are others, however, which metastasize rapidly and widely and kill the patient within a few months. Some of these are irregular enough microscopically to be considered as cancerous, but others appear more innocent than do some of the more bizarre growths which remain localized. Like carcinoma of the exocrine portion of the pancreas islet cell tumors also arise



FIG. 328.—Islet cell adenoma of the pancreas same case illustrated in figure 327. $\times 100$

from ductal epithelium. The method of *spread* of the malignant growths and the sites of metastases are the same as in carcinoma of rest of the gland.

The *diagnostic triad* for islet cell tumor is clinical attacks of hypoglycemia, blood sugar below 50 mg per cent and relief of symptoms by administration of carbohydrates. *Treatment* is surgical excision. The *prognosis* in cases with benign tumors is good, but in those with cancerous ones it is poor. Before leaving this subject, it should be pointed out that in a certain proportion of cases an adenoma cannot be found at the time of surgical exploration. In such instances, the surgeon usually removes the body and tail of the pancreas. The pathologist may find hypertrophied or normal islets of Langerhans. In the latter case, there may be a tumor in an aberrant pancreas or it has been postulated that there may be an increase of individual beta cells scattered between the cells of the pancreatic acini or ducts. When no tumor is found surgical removal

The stroma is usually abundant, dense and hyalinized but it may be scanty, loose and well-vascularized. As a rule, it is infiltrated with plasma cells, lymphocytes and monocytes. Carcinoma of the pancreas *spreads* by contiguity, lymphatics, blood vessels and perineural spaces. Although no organ is immune the most common secondary deposits are found in regional lymph nodes, liver, peritoneum, lungs, gallbladder, diaphragm, mediastinal nodes and pleura.

The *diagnosis* is sometimes difficult to establish, especially in cancer elsewhere than in the head. The only symptom that such patients may have is persistent severe epigastric pain and, because all clinical studies are often negative, they are frequently dubbed as neurotics. Other patients may complain only of persistent fever. The one effective *treatment* is surgical excision, which in growths of the head consists of a pancreaticoduodenectomy. The *prognosis* is grave. The duration of the disease from onset of symptoms to death is 1 to 12 months with an average of 2.5 months.



FIG 327 —Islet cell adenoma of the pancreas
Approximately natural size

Islet Cell Tumors.—These tumors are usually adenomas, less commonly carcinomas and are important because many are associated with hypoglycemia. From the onset, however, it should be emphasized that *hypoglycemia* is not synonymous with hyperinsulinism, and that other conditions besides adenoma or carcinoma of the islet cell type are accompanied by subnormal blood sugar levels. Some of these are lesions of the anterior lobe of the pituitary, adrenal cortical deficiency, hypothyroidism and massive destruction of hepatic parenchyma. Islet cell tumors have been estimated to occur once in every 1000 necropsies but to be associated with hypoglycemia in only 20 per cent of cases. They

affect males twice as frequently as females and occur at all ages with a preponderance between thirty and fifty years. *Symptoms* when present are those of insulin shock or hypoglycemia and consist of headache, weakness, dizziness, nausea, sweating, tachycardia, hypothermia, diplopia, hunger or convulsions. The blood sugar is below 50 mg. per cent and the manifestations are quickly relieved by the administration of carbohydrates.

Most of the *tumors* are in the tail, but they also occur in the body, neck and head. They are single in 90 per cent of cases and multiple in 10 per cent. They are sharply circumscribed, often encapsulated, round or oval, pink grey, brown or hemorrhagic, homogeneous, relatively soft and usually measure from 1 to 2 cm. in diameter, but range in size from 0.1 to 15 cm. (Fig. 327). Less frequently, they are firm and on section are hyalinized, coarsely trabeculated or even calcified. *Histologically*, they are composed of anastomosing cords, clumps or acini of polyhedral pyramidal or cuboidal cells (Fig. 328). They possess a moderate amount of homogeneously eosinophilic or

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of a portion of the pancreas rarely rids the patient of symptoms.

Mechanical Disturbances.—Under this heading will be included only two disorders—rupture and calculi.

Rupture.—Rupture of the pancreas occurs as a *result of* (1) penetrating wounds such as caused by bullets, shrapnel, knife and bayonet and (2) blunt trauma produced by kicks, blows, severe compression between vehicles and automobile accidents. The injury may consist of a bruise, partial tear or complete tear and the resulting *complications* include (1) acute pancreatitis, (2) hematoma around the pancreas, (3) hemorrhage into the lesser or greater peritoneal cavity, (4) acute peritonitis and (5) pseudocyst. Treatment in the more severe cases consists of repairing the damage.

Calculi.—This includes single or multiple stones found in the ducts, and a more widespread process that is known as calcinosis or diffuse calcification of the pancreas. The *cause* is unknown. By some, the primary factor is thought to be stasis produced by squamous metaplasia of ductal epithelium or by chronic inflammation. The resulting exfoliated cells and other detritus which accumulate in the ducts, ductules and acini acquire calcium carbonate and phosphate and thus form the calculi. By others, the process is considered to be merely a progression of fat necrosis that is consequent to acute pancreatitis. Clinical *manifestations* are variable. They consist of epigastric pain, loss of weight, diarrhea, fatty stools, asthenia, diabetes and jaundice (due to compression of the common bile duct or due to impaction of a stone in the ampulla of Vater).

The *process* discloses a diffuse calcification of the pancreas with or without stones in the ducts or stones in the ducts without involvement of the parenchyma. The calculi are single or multiple, smooth, rough, faceted, branched, grey or brown and measure as much as 3 cm. in diameter. They decrease in frequency from the head of the organ to the tail. In the diffuse variety the ducts are filled with sand or gravel, or the deposits may be encrusted upon their walls to produce patent pipestem cord-like structures. In addition, the parenchyma is filled with crumbly chalk-like deposits. In either type the remaining ducts are elongated, distorted and cystic. The parenchyma is grey, firm and fibrous and there may or may not be associated abscesses. *Histologically*, aside from the calcification, there is a diffuse interstitial fibrosis accompanied by a varying degree of chronic inflammatory reaction. Gradually, the acini and later, the islets of Langerhans disappear. The condition is frequently associated with cholecystitis, cholelithiasis and hepatic cirrhosis.

The *diagnosis* of calculi or diffuse calcification of the pancreas can usually be established roentgenologically for the deposits ordinarily contain enough calcium to be radio-opaque. Medical *treatment* consists of administration of pancreatic enzymes and attention to the diabetes when it is present. Surgical treatment consists of removal of the stones or, if the process is diffuse and attended by unbearable pain, of excision of the involved portion of the pancreas. The operative *mortality* is about 10 per cent. Death in untreated cases results from intercurrent infection especially tuberculosis.

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but tend to become less conspicuous with increasing years and during the course of debilitating illnesses. The medulla consists of freely anastomosing cords of lymphoid cells that are separated by the medullary sinuses.

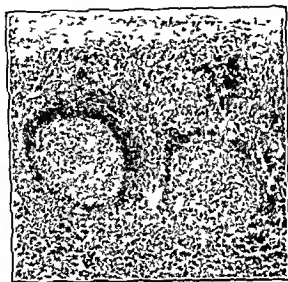


FIG. 329.—Normal lymph node showing moderately well developed lymphoid follicles.
X 50

PATHOLOGY

Congenital Anomalies—Since lymph nodes and lymphatic channels are so changeful in number and position it is not permissible to speak of such variations as abnormal. About the only important developmental anomaly is a tumor of lymphatic channels which is known as *lymphangoma*. This was considered in detail in Chapter I (p. 19).

Inflammations—Inflammatory lesions of lymph nodes may be divided into (1) non-specific which includes acute lymphadenitis, chronic lymphadenitis, mesenteric lymphadenitis, infectious mononucleosis and infectious lymphocytosis and (2) specific or *granulomatous* which includes filariasis, tuberculosis, syphilis, Boeck's sarcoid, tularemia, brucellosis, lymphopathia venereum, actinomycosis, histoplasmosis, sporotrichosis, coccidioidomycosis and a group of metabolic diseases (which also affect the spleen and other organs) known as *Gaucher's disease*, *Hand-Schüller-Christian's disease*, and *Niemann-Pick's disease*. The latter constitute a group of lipid storage diseases wherein the reticulo endothelial system throughout the body becomes loaded with kersin (Gauchers), cholesterol and cholesterol ester (Hand-Schüller-Christian's) and phospholipid (Niemann-Pick's). *Histologically*, the involved organs and tissues disclose large polyhedral sharply defined phagocytic cells, the cytoplasm of which is filled with finely granular lipid material. Although there are certain minor microscopic differences among the cells in the different diseases, the only certain way of differentiating them

Chapter XVI

LYMPHATIC SYSTEM AND SPLEEN

LYMPHATIC SYSTEM

EMBRYOLOGY

THE *lymphatics* originate along the main venous trunk as spaces in the mesenchyme. Dilatations of the networks produce (1) two jugular sacs from which develop lymphatics to the head, neck and arms, (2) a cisterna chyli and retroperitoneal sac which sends lymphatics to the mesentery and (3) two posterior sacs that develop along the sciatic nerves and give origin to the lymphatics supplying the hip, back and legs. *Lymph nodes* develop at three months along the course of the sacs and the peripheral channels from adjacent mesenchyme. Proliferation and differentiation of the latter result in the formation of nodular lymphoid masses which crowd the vessels outwardly to constitute the peripheral sinuses. Condensation of surrounding connective tissue forms a capsule from which trabeculae spread centrally. Medullary cords are formed early but the cortical nodules or follicles with germinal centers are not completed until after birth.

ANATOMY

Lymph nodes are small bean-shaped bodies situated along the course of lymphatic channels. Afferent vessels carrying lymph enter the node along the convex border, and efferent vessels emerge from the flat surface or hilum. The latter also contains arteries and veins which enter and leave the parenchyma. On section, the node discloses an outer lighter rim called the *cortex* and an inner darker portion called the *medulla*. The efferent lymphatics unite to form larger trunks which empty into the right lymphatic duct or thoracic duct, and these drain into the venous system at the junction of right subclavian and internal jugular veins and left subclavian and internal jugular veins respectively. The *right lymphatic duct* receives afferents from the right side of the thorax, the right upper extremity and the right side of the head and neck, whereas the *thoracic duct* drains the rest of the body.

Histologically, the afferent vessels are seen to pierce the capsule and empty into the subcapsular sinus. From here the lymph enters sinuses within the lymph node proper. These are tortuous spaces with perforated walls that are formed of reticulum and phagocytic cells lining fine reticulum fibers. At the hilum they coalesce to form the efferent vessels. The cortex of the node is composed of nodules or follicles which contain germinal or reactive centers (Fig. 329). These are composed of reticulum or stem cells that mature into lymphoblasts, and these in turn are pushed peripherally as they are transformed into lymphocytes. Follicles are prominent in youth,

medulla are enlarged, less cellular than normal, have dilated sinuses and disclose an increase of reticulum, reticulum cells and mononuclear cells. In other cases the reticulum is transformed into irregular masses of hyalinized fibrous tissue that replace varied portions of the gland and, thereby, distort the normal architecture.

Non-specific Mesenteric Lymphadenitis—This inflammation has been reported as occurring in as many as 6 per cent of all surgically treated patients. It is most prevalent in the first and second decades of life after which it tapers off rapidly. *Clinical manifestations* consist of acute abdominal pain that may or may not be confined to the right lower quadrant, and occasionally of leukocytosis. There may be tenderness over the right lower quadrant but the resistance and rigidity of acute appendicitis are usually absent. The condition, nevertheless, cannot be distinguished with certainty from acute inflammation of the vermiform process.

Grossly, the nodes of the mesentery, especially those opposite the terminal ileum, are enlarged, single and sharply demarcated or less frequently, they are fused into large, bulky, bossed, irregular masses with small or large central abscesses. In the latter instance there is usually suppuration of the surrounding connective and fat tissue and sometimes the process extends through the serosa to produce a localized or generalized peritonitis. *Histologically*, the changes vary from medullary edema and neutrophilic infiltration to frank abscess formation and are, therefore, similar to the acute infections of peripheral nodes already described.

The cause of mesenteric lymphadenitis is not always apparent, but is generally believed to result from infections or abrasions of the terminal portion of the small intestine. At other times, it follows an acute pharyngitis and is then thought to be due to absorption by the prominent lymphoid patches in the terminal ileum of bacteria swallowed with the sputum. As already stated, the condition can not be differentiated from acute appendicitis and such patients are, therefore, usually operated upon. As a rule, the vermiform process is removed but no other surgical interference is necessary.

Infectious Mononucleosis—This is also known as glandular fever. Its cause is unknown. The disease has been reported as reaching epidemic proportions but is not highly contagious. It is more common in males and is most prevalent around the twentieth year of life. *Symptoms and signs* are quite variable and consist of combinations of sore throat, fatigue, headache, coryza, malaise, gastrointestinal disturbances, dull, soreness of the eyes, cough, sweating and dizziness. Peripheral lymph nodes are enlarged in about 84 per cent of cases and the spleen is palpable in about 50 per cent of cases. The leukocytic count rarely reaches 20,000 per cubic millimeter of blood, the neutrophils number less than 40 per cent, and there is a preponderance of atypical lymphocytes. At one time these were thought to be monocytic cells and hence the name. Aside from the peripheral blood picture, a positive heterophile antibody reaction (agglutination of sheep cells by the patient's serum) confirms the diagnosis.

is by chemical analysis of involved organs or tissues. The *mycotic* lesions and *Boeck's sarcoid* have been considered in connection with the skin, and *lymphopathia venereum* has been described under diseases of the anus. *Brucellosis*, caused by the *Brucella* group of organisms, produces in the lymph nodes a diffuse lesion that resembles the granulomatous type of Hodgkin's disease. *Tularemia*, caused by *B. tularensis*, is manifested in the acute stages by small focal areas of necrosis composed of detritus and nuclear fragments. These are surrounded by neutrophils and mononuclear cells. In the chronic stages the periphery is encompassed by epithelioid cells, fibroblasts and Langhans' giant cells. The lesion may, therefore, be easily mistaken for tuberculosis. The non-specific inflammatory lesions, filariasis, tuberculosis and syphilis will be considered at greater length.

Acute Non-specific Lymphadenitis.—This is a common affliction. It is found in any part of the body, but is clinically most apparent in peripheral nodes and is due to an inflammation of lymph nodes that drain an infected, abraded or otherwise traumatized area. Two of the most common sites are the cervical and submental regions from infections in the tonsils, pharynx and mouth. The nodes are enlarged, discrete, soft, tender and painful. They rarely measure more than 1.5 cm. in diameter and on section are bulging, moist and pink to grey. Sometimes they may contain small yellowish foci. *Histologically*, the follicles are prominent, chiefly because they are spread apart by an accumulation of edema fluid in the medullary cords. The sinuses too are distended and the entire medulla is, therefore, less cellular than normal. There is a relative increase of phagocytic cells and neutrophils. When the infection is severe, the latter flood the tissue and may collect in small foci to form abscesses. These in turn may coalesce until the entire node is converted into a pocket of pus. Healing occurs by resolution in mild infections and by fibrosis in infections attended by suppuration.

Chronic Non-specific Lymphadenitis.—This is as common as the acute form of inflammation. It too occurs in nodes that drain chronically infected or abraded areas. Such nodes are frequently seen in the groin from clinically troublesome or non-apparent lesions in the distal portions of the lower extremities. Other common locations again are the submental and cervical regions particularly in cases of ulcerating carcinoma of the mouth, tonsils and pharynx. In fact, chronic lymphadenitis is so frequent under these circumstances that one should always be careful in construing all small nodal enlargements as cancerous, for the likelihood is that they are inflammatory. Chronically, infected lymph nodes are, as a rule, larger than acutely infected ones. They are, nevertheless, usually discrete, movable, firm and ordinarily not tender. *Grossly*, they are surrounded by a fibrous tissue capsule; they may or may not cut with increased resistance, and the surfaces are either homogeneously pink or they are grey and traversed by irregular depressed scars. *Histologically*, they may show an increase in number and size of the follicles which are situated about the periphery of the node and do not invade the medulla. The interfollicular spaces and

by a single discrete subcutaneous nodule which slowly enlarges and fuses with its neighbor and the skin to produce an irregularly bossed mass. In time, the center softens, caseates and liquefies, the skin becomes devitalized, and numerous sinuses are formed with the surface of the neck. Mediastinal enlargement may be associated with fever, loss of weight, anorexia, and because of compression of the trachea and bronchi, with a dry cough. The nodes may involve the left recurrent laryngeal nerve, erode into the trachea and bronchi to produce a fistula between these organs, or result (by contraction) in an esophageal diverticulum. Tuberculosis of mesenteric nodes



FIG. 330.—Tuberculous lymphadenitis. There are areas of caseation surrounded by massive fibrosis.

may be associated with fever, abdominal distention and general debility, or more frequently, they are completely asymptomatic and the only evidence of previous infection is calcification.

Grossly, the localized form of nodal tuberculosis is similar to that already described in the neck. As the process heals, there is a gradual replacement of the structures by dense fibrous tissue and later still by calcification (Fig. 330). Histologically, the acute lesions are composed of small tubercles or of large areas of necrosis surrounded by tubercles and tuberculous granulation tissue. The generalized form of lymph node tuberculosis, when of the miliary type, shows none or only moderate enlargement of the nodes. They are relatively soft and on section may show minute grey foci. His-

Ordinarily, there is no recourse to a lymph node biopsy but in obscure cases one may have the opportunity to examine a specimen that was inadvertently removed. The *histologic* changes consist (1) a persistence or central disruption of the follicles, (2) a swelling of the cords by small and large lymphocytes, reticulum cells, phagocytes, eosinophils and infectious mononucleosis cells (large round cells with basophilic granular or vacuolated cytoplasm and round or slightly indented eccentric nuclei), (3) a compression and distortion of the sinuses and a filling of their spaces with cells similar to those in the cords, (4) an increase of reticulum and (5) increase of vessels and a proliferation of their endothelium.

There is no specific therapy and the *prognosis*, except for the rare case of rupture of the spleen, is excellent.

Infectious Lymphocytosis.—This inflammation appears to be closely allied with infectious mononucleosis. It occurs in children in the first decade of life and is characterized by a peripheral leukocytic count that reaches as high as 100,000 per cubic millimeter with over 90 per cent of the cells mature and normal lymphocytes. Many patients are without *clinical manifestations*, while others may disclose a sore throat and fever that lasts for a few days. Lymph nodes and spleen are not enlarged and the heterophile antibody reaction is negative. *Histologic* changes that have been described in lymph nodes consist of a blotting out of some follicles and central hyalinization of others, and a proliferation of the reticulo-endothelial cells of the sinus. The disease is thought to be caused by a virus and it runs its course in three to five weeks.

Filariasis.—Filariasis refers to infestation by *filaria Bancrofti*. The adult worms are found in the lymphatics and lymph nodes where, because of direct obstruction or of obstruction resulting from consequent inflammation, they produce *lymphedema* (elephantiasis). The lesion is a *granuloma* found in the perilymphatic, perinodal, intralymphatic and intranodal, areas. It consists of small collections of epithelioid cells surrounded by lymphocytes and occasionally Langhans' giant cells. Between these "tubercles" there is a progressive increase of fibrous tissue. The organisms when found are sometimes surrounded by eosinophils, while at other times they are encompassed by a zone of necrosis which is walled off by epithelioid cells and giant cells.

Tuberculosis.—Tuberculosis of lymph nodes can occur anywhere in the body. The process may be localized to a single node or group of nodes or it may be disseminated throughout most or all of the nodes. It occurs at all ages but is most prevalent in the third decade of life; it is more frequent among the lower classes, and it attacks both sexes. *Symptoms* and *signs* depend upon the type and extent of the infection. In the *generalized form*, they mimic Hodgkins' disease, if the lesions are of the hyperplastic or fibrous type, or they are part of a widespread miliary process. The *localized disease* is most frequent in the cervical, mediastinal or mesenteric nodes and the portals of entry are the mouth and pharynx, lungs and small intestine respectively. Cervical lesions are manifested

Sometimes, however, the cellular pattern is such as to defy precise classification. At other times one node or a portion of a node may show one type of histologic pattern while a portion of the same node or another node from the same patient may show an entirely different picture. Thus we have encountered a patient who at one time revealed a histologic picture of lymphosarcoma, several years later disclosed one of Hodgkin's disease and at autopsy showed not only lymphosarcoma and Hodgkin's disease but also reticulum cell sarcoma. We have also encountered other cases that initially disclose histologic patterns of lymphosarcoma and subsequently died of Hodgkin's disease. Furthermore, it is common experience for a lymphosarcoma to terminate as lymphatic leukemia and cases have been recorded of lymphatic leukemia associated with reticulum cell sarcoma and with Hodgkin's disease.

Those working with *tissue cultures* have had the same experience. A node or portion of a node may at one time yield a growth that is considered characteristic of Hodgkin's disease, while another portion of the same node or a node removed from a different area at the same or a subsequent time will disclose what is regarded as typical of lymphosarcoma.

Finally, from the *biochemical* point of view F. R. Miller has isolated a myelokentric acid from the urine of patients with myeloid leukemia, lymphoid leukemia, monocytic leukemia and Hodgkin's disease and a lymphokentric acid from the urine of patients with lymphoid leukemia, lymphosarcoma, myeloid leukemia, monocytic leukemia and Hodgkin's disease. Myelokentric acid stimulates myelopoiesis and matures lymphoid cells whereas lymphokentric acid stimulates lymphopoiesis and matures myeloid cells. Miller has further shown that by reduction, myelokentric acid is convertible into lymphokentric acid and by oxidation, lymphokentric acid is convertible into myelokentric acid. It thus appears that the different entities grouped under the title lymphoblastomas are closely related.

Despite this close association there are some differences between the various diseases particularly with regards to longevity and prognosis, so that it behooves one to *classify* them whenever possible. The grouping which we, at the Jefferson Hospital, use and find quite satisfactory is as follows: (1) leukemia, (2) leukosarcoma, (3) reticulum cell sarcoma, (4) Hodgkin's disease, (5) lymphosarcoma and (6) giant follicular lymphoblastoma. *Leukemia* may be defined as an invariably fatal disease of the hemopoietic organs which at one time or another discloses immature leukocytes in the peripheral blood. Clinically, it exists in the leukemic and aleukemic or subleukemic stages. There are three main *varieties*—lymphocytic, myelocytic and monocytic. The lymph nodes in each of these, while not necessarily enlarged, disclose characteristic changes. In lymphocytic leukemia, they are flooded with lymphocytes or lymphoblasts, in myelocytic leukemia, they reveal a proliferation of mature or immature myeloid cells, and in monocytic leukemia, the normal pattern is replaced with monocytic cells. Since leukemias are not surgical problems and since the surgical patholo-

tologically, the lesions consist of the "soft tubercle." In the chronic type of disseminated tuberculosis the nodes are enlarged, firm, matted, fibrous and closely resemble Hodgkin's disease. Histologically, there are solid or caseating tubercles usually associated with considerable fibrosis.

The *diagnosis* of superficial nodes is made by biopsy, or by culture or guinea pig inoculation of aspirated material. Such nodes can be excised surgically or treated radiologically. *Treatment* of deep nodes is medical.

Syphilis.—Syphilis may produce enlargement of the lymph nodes in the primary, secondary or tertiary stages. In the *primary* stage, the nodes involved are those that drain the chancre. The changes are those of acute non-specific lymphadenitis without suppuration. In *secondary* syphilis, they resemble the hyperplastic type of chronic lymphadenitis. The follicles are enlarged and increased in number. The interfollicular cords and medulla show dilated sinuses, proliferation of reticulum and reticulum cells, infiltration with monocytes and some fibrosis. Silver impregnation reveals numerous treponema pallida. The lesions in *tertiary* syphilis are identical with similar lesions in other organs and are, therefore, of the diffuse granulomatous or of the gummatous variety.

Tumors.—Neoplasms of lymph nodes may conveniently be divided into primary and secondary.

Primary Tumors.—Primary tumors or tumor-like conditions constitute about 5 per cent of all malignant growths. Because of the chaos that exists in the medical literature with regards to classification, the entire group is often referred to as the *lymphoblastomas* or malignant lymphomas. Such a caption seems to be justified not only because the clinical manifestations and course are strikingly similar, but also because the seemingly distinct entities which comprise the group are doubtlessly related histogenetically, morphologically, culturally and biochemically. Evidence for this relationship may be briefly outlined as follows.

Histogenetically, there are two theories regarding the origin of blood cells, namely, the monophyletic which holds that there is a common progenitor for all the different series, and the polyphyletic which holds that each series has a separate parent cell. Regardless of which view is correct, since lymph nodes and bone marrow arise directly from mesenchyme and since the various series of cells develop within this primitive mass, there must ultimately be a common cell which serves as the progenitor. Whether this cell is the immediate precursor of the lymphocytic, myelocytic, monocytic, erythrocytic and megakaryocytic series of cells or whether it passes through half a dozen intermediate stages appears to be of academic interest only. The important thing to remember is that there is such a cell, that it may be called a reticulum cell, an undifferentiated mesenchymal cell or a stem cell, and that when properly stimulated it gives rise to a single series or several series of leukocytic cells.

From the *morphologic* point of view, as described below, the various diseases can ordinarily be placed into one group or another.

At *postmortem*, the deep lymph nodes are affected more frequently and more extensively than are the superficial ones, and the abdominal retroperitoneal and para-aortic ones involved more often than the mediastinal. Initially, the nodes are small discrete and relatively soft. As they enlarge, they tend to mat and form irregularly bossed, firm masses that may measure as much as 20 cm in diameter. Under these circumstances, the capsules become indistinct, penetrated and finally obliterated, and the tumor tends to infiltrate adjoining structures. Cut surfaces are usually homogeneously, grey, pink, somewhat bulging and encephaloid (Fig 331).

In some cases of Hodgkin's disease, however, they tend to be greyish white and fibrous, while in others, they present varying degrees of necrosis and hemorrhage. Also, in some cases of giant follicular lymphoblastoma the surfaces are honeycombed rather than homogeneous and the follicles can be seen with the naked eye. Aside from lymph nodes, the lymphoblastomas may involve any organ or tissue in the body. These deposits may be secondary, or they may be primary and represent the only manifestation of the disease. The organs most frequently affected are the spleen, liver, bones, lungs, and gastrointestinal tract. The lesions may exist as diffuse infiltrations but most often occur as nodules of varying sizes that appear similar to the enlarged nodes. As already stated, the histologic patterns are ordinarily quite distinct and the different diseases will, therefore, be briefly considered separately.



FIG 331—Lymphoblastoma. This greatly enlarged node was from a case of Hodgkin's disease but grossly it cannot be differentiated from any of the other members of the group.

Reticulum cell sarcoma represents the most primitive of all lymphoblastomas. The literature on this subject, however, is quite confused, mainly because different authors have different ideas as to what constitutes a reticulum cell. As already pointed out, this author does not or, to be more accurate, cannot differentiate it from the primitive mesenchymal or stem cells of other writers, and, therefore, in this book the terms are used synonymously. Under such circumstances, reticulum cell sarcoma is the least common of all the lymphoblastomas. *Histologically*, the normal follicular architecture is completely replaced with a diffuse infiltration of primitive cells. These vary considerably in shape and size. They are round, oval, irregular, triangular, elongated or hexagonal and are two to four times the diameter of ordinary lymphocytes (Fig

gist is not ordinarily called upon to examine nodes from such patients (because the diagnosis is made by blood smear) the subject will not be pursued further. *Leukosarcoma* is reserved for those cases in which there is a local infiltrating tumor in conjunction with an initial normal hemogram but with a terminal picture of leukemia. The tumor (and leukemia) may be (1) lymphoid consisting of lymphocytic or lymphoblastic cells, (2) myeloid consisting of mature or immature cells of the granulocytic series and (3) monocytoid consisting of mature (monocytic) or immature (monoblastic) cells. Of the three varieties, the lymphoid type is by far the most common, but since the histologic picture is indistinguishable from lymphosarcoma it will not be considered further.

Reticulum cell sarcoma, *Hodgkin's disease*, *lymphosarcoma*, and *giant follicular lymphoblastoma* are often indistinguishable clinically and, except for the histopathologic changes, will, therefore, be discussed together. The causes of the disorders remain unknown. It is generally conceded that all except Hodgkin's disease are true neoplasms, but many authors still regard Hodgkin's disease as a granulomatous lesion. It is the author's opinion that the condition should be classed as a true tumor (1) because its course parallels that of the other lymphoblastomas, (2) because its local growth characteristics are those of a genuine neoplasm and (3) because the lesion often grades over to a frankly sarcomatous type of growth or is transformed into an outright reticulum cell sarcoma. The question whether lymphoblastomas are of multicentric origin or whether they are of monocentric origin and involve other organs and tissues by metastasis is not settled. Perhaps both contentions are correct. At any rate, it is known that some cases appear to disclose multiple lesions synchronously, others show them metachronously and others still appear to have a single lesion confined to a group of nodes or to a single organ. There are many recorded cases of the latter that have been cured by surgery alone.

The *clinical manifestations* of the group of lymphoblastomas under discussion are quite protean. Although in each disease a large group of cases may show a slight difference in age and in the order in which symptoms and signs appear, there is no clinical way of distinguishing the different processes in any given case. As a group they can occur at any age but the majority are between the third and sixth decades with an average of forty-three years. Males are affected about three times as frequently as females. The most common single symptom is a painless enlargement of superficial lymph nodes. As a rule, cervical nodes are involved but the swelling may be confined to axillary or inguinal nodes or it may be generalized. The remaining manifestations may be systemic or localized depending upon the organs or structures involved. Among others the following may be listed: anorexia, weakness, loss of weight, chills, itching, fever, sweating, cough, dyspnea, expectoration, hemoptysis, abdominal pain, abdominal swelling, constipation, diarrhea, hematemesis, jaundice, pain in the bones, splenomegaly, hepatomegaly, ascites, peripheral edema, anemia and neutrophilic leukocytosis.

cells, neutrophils, monocytes, eosinophils and Sternberg-Reed cells (Fig 333). These are giant cells that measure 15 to 40 microns in diameter. They are of irregular shapes, often with processes attached to the reticulum. The cytoplasm is abundant to scanty and acidophilic or basophilic. The nuclei are single or multiple and "piled up." Their borders are lobulated and distinct and their chromatin is clumped. They are the pathognomonic cells. Without them, a diagnosis of Hodgkin's disease cannot be made. In addition to the aforementioned cells, there is often an increase of reticulum cells and of reticulum fibers. Sometimes,

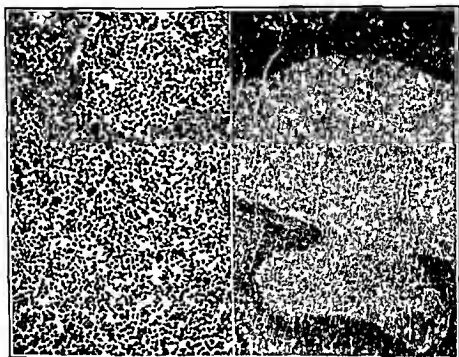


FIG 334

FIG 335

FIG 334—Lymphosarcoma. The cells are all mature lymphocytes. $\times 100$

FIG 335—Giant follicular lymphoblastoma showing a portion of an enlarged follicle. $\times 37.5$

fibrosis becomes extreme and at other times, there is massive necrosis and extensive hemorrhagic extravasation.

Lymphosarcoma is about as common as Hodgkin's disease and both constitute most of the lymphoblastomas. There are two types—*lymphocytic* and *lymphoblastic*. In each the normal architecture, as in other lymphoblastomas, is erased. In the lymphocytic variety, the entire structure is densely infiltrated with mature lymphocytes (Fig 334). These are small round cells slightly larger than erythrocytes. They have a scanty basophilic or imperceptible cytoplasm and uniformly staining round nuclei. Lymphoblasts on the other hand are one and a half to two times this size. Their cytoplasm, although scanty, is more abundant and the nuclei are larger, less dense and more granular. In each type mitoses may

332). Their borders are sometimes sharply defined, but at other times fade away gradually. Frequently, they are aligned upon, or possess processes that are attached to, a fine reticulum. The cytoplasm, as a rule, is abundant, basophilic or acidophilic and homogeneous. The nuclei are single, rarely double, round, oval, lobulated or irregular and may be in a state of mitosis. Their borders are distinct and their chromatin is clumped and coarse. There is little or no fibrosis or necrosis. The reticulum is best demonstrated by silver impregnation.

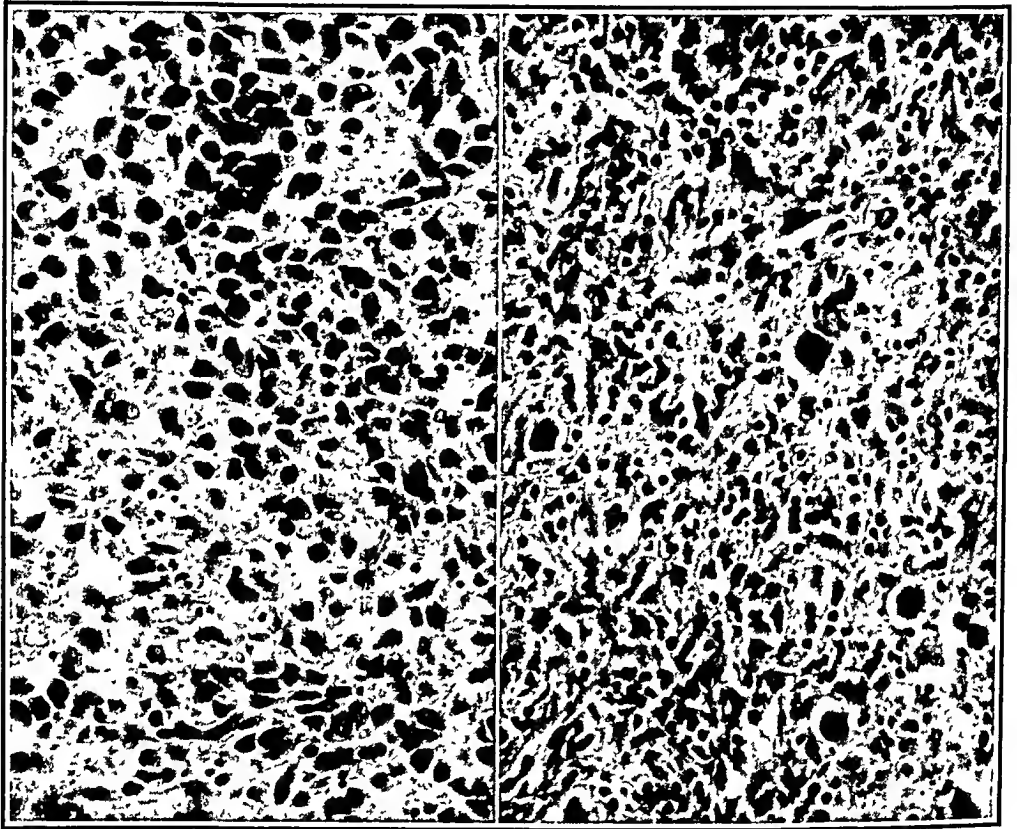


FIG. 332.

FIG. 333.

FIG. 332.—Reticulum cell sarcoma showing large polyhedral or elongated cells with abundant cytoplasm, large round or oval nuclei and scattered mitoses $\times 100$.
 FIG. 333.—Hodgkin's disease illustrating numerous Steinberg-Reed giant cells and massive fibrosis Same node shown in figure 331

Hodgkin's disease is often divided into a *sarcomatous* and a *granulomatous* variety. The former is uncommon, more malignant and, in addition to containing some foci of the granulomatous type, discloses a marked proliferation of cells that are identical with the reticulum cells just described. It, therefore, appears that this variety, is nothing more than the granulomatous form which is being, or has become, transformed into a reticulum cell sarcoma. Once again this demonstrates the close relationship among the lymphoblastoma group of diseases. The *granulomatous* variety is the usual picture encountered in Hodgkin's disease. Histologically, there is a complete loss of the normal nodal architecture and a diffuse infiltration with varying numbers of lymphocytes, plasma

mistaken for a lymphoblastoma, (2) when the primary neoplasm is ulcerated and infected enlargement of draining lymph nodes may be due to inflammation and not to neoplastic involvement, (3) carcinoma invades the nodes much more frequently than sarcoma, (4) the diagnosis can often be established by aspiration or incisional biopsy and morphologic evidence of tumor is mandatory, (5) treatment in widespread or surgically inaccessible masses is irradiation, and in localized metastases it is wide surgical excision, irradiation or both, and (6) the prognosis is hopeless in skip or generalized metastases but may be fair if the disease is confined to the draining nodes.

Mechanical Disturbances—There are only two important lesions of lymphatic vessels and nodes in this category—rupture and obstruction. *Rupture* of the main trunks in the abdomen and thorax results in chylous ascites and thorax respectively. The lesions are important because they produce rapid cachexia. They are fortunately rare. Much more common is *obstruction* to the flow of lymph. This usually occurs in the extremities and less often in the external genitalia, and results in marked swelling of the affected part to produce what is called *lymphedema* (elephantiasis). The causes of obstruction may be listed as follows: (1) *Congenital*. This may be divided into familial (Milroy) where there is swelling of one or both lower extremities at birth, and congenital but not familial where the swelling starts in childhood but is not present at birth. (2) *Inflammatory*. This may be due to filaria bancrofti, streptococci, trichophytosis, tubercle bacilli, etc. The infection may be single or recurrent and produces both cellulitis and lymphangitis. (3) *Neoplastic*. This usually results from occlusion of the lumen by tumor cells, the best example of which is carcinoma of the breast. Rarely does external pressure by a tumor cause lymphedema. (4) *Mechanical*. The most common example of this is lymphedema of the upper extremity following a radical mastectomy. Since severance of the axillary vessels in animals does not result in swelling of the limb, it is thought that the actual cause is a low grade cellulitis and angitis, or the fibrosis that follows irradiation. Once the process is initiated, stagnation of lymph predisposes to infection which results in fibrosis and this in turn causes more obstruction. Lymphedema often starts as a puffiness around one of the joints which with elevation of the extremity tends to disappear. Gradually but inexorably, it increases in size and severity until the limb becomes many times its normal size. The skin becomes thick and indurated, and the swelling becomes resistant to pressure. *Histologically*, the skin is thick and hypertrophied, the fat is replaced with dilated lymphatic spaces and fibrous tissue, the muscles and nerves are atrophied, and the dermal appendages are infiltrated with neutrophils and lymphocytes. The only effective *treatment* is surgical excision of long strips of skin and underlying tissue performed in multiple operations. Bandages are used postoperatively for support and to facilitate the flow of lymph. Operation is, of course, contra-

be found; there is no increase of reticulum or fibrous tissue, and there is no necrosis or hemorrhage. This histologic pattern is indistinguishable from that in lymphocytic or lymphoblastic leukemia or leukosarcoma.

Giant follicular lymphoblastoma is characterized by an increase in number and size of the lymphoid follicles (Fig. 335). As the name implies, these are of giant proportions so that one follicle alone may occupy several low power microscopic fields. The follicles are composed of reticulum cells in the center, lymphoblasts beyond these and lymphocytes at the periphery. Because of their enlargement, the interfollicular tissue is usually compressed. It shows an increase of reticulum, disappearance of the sinuses and a diffuse infiltration with mature lymphocytes. Less often the follicles are separated by broad sheets of lymphocytic cells. It might be appropriate at this point to list some of the many *names* applied to giant follicular lymphoblastoma. They are: giant lymph follicle hyperplasia, malignant lymph follicle hyperplasia, follicular lymphoblastoma, giant follicular lymph adenopathy, follicular lymphadenoma, follicular lymphoma, Brill-Symmer's disease, etc. It is the least malignant of all lymphoblastomas and when it terminates with the death of the patient, it may remain in its initial form or it may be transformed into lymphosarcoma, lymphatic leukemia, Hodgkin's disease or reticulum cell sarcoma. Once again this shows the close relationship among the lymphoblastoma group of diseases.

A proper *clinical evaluation* of the lymphoblastomas can only be made after all available data is gleaned from the internist, hematologist, roentgenologist and pathologist. In no other single group of diseases is this so important. *Treatment* consists of (1) radical surgical extirpation followed by irradiation, when the lesion is accessible and confined to a localized area or organ, (2) irradiation when the disease is generalized or beyond the scope of surgical excision and (3) chemotherapy. One of the drugs in vogue at the time of writing is nitrogen mustard. At present, however, all that can be said for nitrogen mustard is that it has a salutary but not curative effect on Hodgkin's disease, lymphosarcoma and lymphatic leukemia. As a rule, the ultimate *prognosis* in lymphoblastoma is poor. This is particularly true for the generalized form of the disease. When the lesions are localized, however, the chances of cure are as good as they are in carcinoma of internal organs. The average survival of patients with giant follicular lymphoblastoma is 4.6 years, of lymphosarcoma and Hodgkin's disease about 2.5 years, and of reticulum cell sarcoma about 6 months.

Secondary Tumors.—These tumors of lymph nodes are much more frequent than primary ones. Since this constitutes a heterogeneous group and since involvement of regional nodes has been commented upon throughout this text, little space will be devoted to the topic here. The following should be emphasized: (1) the metastases may be local, skip or distant and solitary, multiple or generalized. When the primary lesion is not apparent any of these may be

PATHOLOGY

Congenital Anomalies—Developmental malformations consist of a *right-sided spleen* in *situs inversus*, variation in size either abnormally large or abnormally small, *absence*, *fissuring* or *lobulation* and *accessory spleens*. Ordinarily, *accessory spleens* are of no clinical significance, but if the patient is subjected to a splenectomy for hemolytic jaundice or primary thrombocytopenic purpura and if accessory spleens are overlooked, they may result in a recurrence of the disease. The incidence of accessory spleens is given as varying from 10 to 35 per cent of all autopsies and as high as 44 per cent of all patients in whom the spleens have been removed. The higher incidence in the latter occurs because the presence of congenital splenic disease prevents the normal disappearance of the accessory organs which are relatively common at birth. The *genesis* of multiple spleens is failure of fusion of the hillocks which are normal before three months of embryonic life. They are usually located in the vicinity of the main organ, namely, at the hilum, in the gastrosplenic ligament, retroperitoneally near the tail of the pancreas and in mesentery of the large and small intestines. Less frequently, they are found within the pancreas, greater omentum, left testicle and left ovary. They vary in number from 1 to 10 and in size from a few millimeters to 2 cm. Histologically, they are identical with the adult organ.

Inflammations—There are only three surgically important infections of the spleen—*acute abscess*, *echinococcus disease* and *tuberculosis*. Echinococcus disease exists in the form of cysts that are identical with those in other organs.

Acute Abscess—Acute abscess of the spleen is reported as occurring in from 0.4 to 0.7 per cent of all autopsies. The most frequent origin is hematogenous metastasis from distant infections such as furuncles, otitis media, erysipelas, thrombophlebitis, appendicitis and salpingitis. Less frequently, it is a sequela of trauma wherein destroyed tissue is invaded by organisms that are transiently carried in the blood stream. Occasionally, it results from extension of infection from neighboring organs. *Symptoms* may not appear for several days or weeks after the inception of the process. There are sudden and severe or gradually appearing pain in the left upper quadrant of the abdomen that may radiate to the left shoulder, chills, fever, leukocytosis, overlying tenderness and muscle spasm, splenomegaly and roentgenographically elevation of the left diaphragm and fluid in the left pleural cavity. The gross and microscopic appearances are similar to those of other acute abscesses. Surgical treatment is confined to those abscesses that are not part of a general pyemia or that do not arise from endocardial vegetations. It consists of splenotomy or splenectomy. The mortality rate in untreated cases is reported as ranging from 80 to 100 per cent.

Tuberculosis—Tuberculosis of the spleen is usually part of a generalized disease, but occasionally, the predominating infection is in the spleen and other lesions are insignificant or undetectable. Such infections are spoken of as primary in the spleen and are anal-

SPLEEN

EMBRYOLOGY

The spleen is first apparent in the 8 mm. stage of embryonic life as a swelling of mesenchyme beneath the mesothelium of the left side of the mesogastrium. Projections of tissue above the surface give several hillocks which fuse and at three months impart to the structure its definitive form. Differentiation of the mesenchyme gives rise to the capsule, trabecles and pulp. The sinuses develop as slits in the mesenchyme and later unite with the vessels. Collections of lymphocytes about vessels at six months give rise to the Malpighian corpuscles or lymphoid nodules.

ANATOMY

The spleen is surrounded on all sides except the hilum by peritoneum. Although changeable, it usually weighs about 140 gm., and measures 10 x 6 x 4 cm. It is flat and oblong. It has two *borders* and a ridge. The anterior border is sharp, notched and separates the convex or diaphragmatic surface from the gastric surface which lies in contact with the stomach and tail of the pancreas. The posterior border is rounded and separates the diaphragmatic from the renal surface which contacts the kidney. The gastric and renal *surfaces* form the flat portion of the spleen and are separated from each other by a ridge. The lower portion of the ridge forms the hilum through which pass vessels and nerves. There are two *poles*—the upper abutting against the vertebra and the lower contacting the splenic flexure of the colon. The lienorenal and gastrosplenic ligaments hold the organ in position. The *arterial supply* comes from the tortuous splenic artery—a branch of the celiac. The *venous drainage* is by way of the splenic vein which unites with the superior mesenteric to form the portal vein. The *nerve supply* is from the celiac plexus, and the lymphatics drain into the pancreaticolienal nodes.

Histologically, there is a capsule which sends projections into the organ that are called trabecles, white pulp and red pulp. The capsule and trabecles are composed of dense connective tissue, elastic tissue and a few smooth muscle bundles. The white pulp consists of regular lymphoid tissue that is disposed about arterioles forming the lymphoid nodules. The red pulp is modified lymphoid tissue. It consists of a meshwork of reticulum fibers that are continuous with those of the white pulp and with the collagenous fibers of the trabecles. The meshes form sinuses that are lined by macrophages and are filled with lymphocytes, free macrophages and cells of the circulating blood. They are continuous on the one hand with the venous capillaries and on the other with arterial capillaries.

lesions. Although they are usually part of a generalized disease, in some cases they appear to be confined to the spleen. *Grossly*, there are, as a rule, no definite distinguishing characteristics. The spleen is slightly to greatly enlarged. The surface is smooth or bossed, the capsule is tense, the edges are rounded, and the consistency is firm. Cut surfaces usually disclose greyish white, moderately firm, bulging, sharply circumscribed or indistinct nodules in varying numbers and of varying sizes (Fig 336). As a rule, the masses are homogeneous but sometimes, those in Hodgkin's disease disclose foci of necrosis and hemorrhage or diffuse fibrosis and those in giant follicular lymphoblastoma reveal a honeycombed appearance. The *histologic* changes are similar to those described under lymph nodes. If the disease is localized to the spleen, *treatment* is splenectomy followed by irradiation therapy. The *prognosis* must always be guarded for dissemination is the rule. The outlook is better in giant follicular lymphoblastoma than in Hodgkin's disease or lymphosarcoma.

Hemangioma—Hemangioma of the spleen is important from the surgical standpoint because it is one tumor that is curable. Its incidence is recorded as ranging from 0.1 to 0.2 per cent of all autopsies. It is said by some to be a congenital anomaly of vessels that grow over a period of years, and by others to represent new buddings and growth of the vascular apparatus. It is found at all ages but is discovered in the majority in the fourth decade of life, and it has no predilection for either sex. *Symptoms* and *signs* consist of swelling of the abdomen, pain in the left upper quadrant, loss of weight, dyspnea, dysphagia, anemia, ascites and splenomegaly. If rupture occurs, there are sudden severe pain, shock and exsanguination. *Grossly*, the tumors range in size from a few millimeters to ones weighing over 13,000 gm and measuring 28 cm in diameter. They are irregularly lobulated, deep red to cyanotic, moderately firm and cystic and, when large, occupy most of the spleen. Cut surfaces reveal a rather solid hemorrhagic tumor or more often a sponge-like mass soaked with blood in which there are often cystic spaces. *Histologically*, the growth is of the capillary or cavernous types. *Treatment* is splenectomy. The *prognosis* is good.

Endothelioma—Endothelioma may be used here to cover tumors that have been termed endothelioma, hemangioendothelioma and angiosarcoma. The literature on this subject is most confusing, and as far as I can determine contains no clear cut distinctions. This group represents the malignant counterpart to hemangiomas. The growths are more common in males and occur at an average age of forty-eight years. *Clinical manifestations* are similar to those in hemangioma except that they are more severe and progress rapidly. The tumors occupy a part or most of the spleen. They occur as numerous elevated, white, grey or hemorrhagic nodules dispersed throughout a red or bluish red parenchyma. *Histologically*, they consist of irregular spaces or capillaries lined with irregular cells that often form papillary masses in the lumens. Their cytoplasm is scanty and the nuclei are relatively large and deeply stained. Between the vessels, there is a diffuse infiltration with similar cells.

ogous, from the clinical standpoint, to tuberculosis of the kidney. Of interest to the surgeon and surgical pathologist is the chronic form of the disease. The optimum age is twenty to forty years, and the *manifestations* consist of pain in the left upper quadrant, anorexia, lassitude, anemia, loss of weight, fever, gastrointestinal disturbances, splenomegaly and often enlargement of the liver. Tuberculosis may or may not be demonstrable in other organs. The *spleen* varies in size from slightly larger than normal to half a dozen times the normal size. The external surface is nodular, hemorrhagic and relatively smooth, or it is fibrotic and attached to adjacent structures by adhesions. Cut surfaces disclose a fibrocaseous process that occupies a portion or all of the organ. To remove an active focus of infection the *treatment* is splenectomy.



FIG. 336.—Lymphosarcoma spleen. There are several circumscribed grey nodules.

Tumors.—Histogenetically, neoplasms of the spleen may be classified as follows: from fibrous tissue of the capsule and trabecles, a fibroma and fibrosarcoma; from smooth muscle of the capsule and trabecles, a leiomyoma and leiomyosarcoma; from lymphoid tissue (reticulum cells), any of the lymphoblastomas already described in connection with lymph nodes; from vessels, a lymphangioma, hemangioma and endothelioma (hemangioendothelioma and hemangiosarcoma); from congenital epithelial inclusions, a dermoid cyst, and from distant areas, metastatic tumors. *Fibroma, fibrosarcoma, leiomyoma, leiomyosarcoma* and *dermoid cysts* are rare, but when encountered, they are no different than similar tumors in other organs.

Of the *lymphoblastomas*, Hodgkin's disease, lymphosarcoma and giant follicular lymphoblastoma are the only important surgical

diseases, or it may be idiopathic. It is probable that those cases recognized in adult life without an apparent cause and termed idiopathic are instances of the *congenital* type that have escaped notice. *Synonyms* for congenital hemolytic jaundice are hemolytic splenomegaly, chronic acholuric jaundice, chronic familial jaundice and spherocytic anemia. The *cause* of the disease is unknown. It affects both sexes with equal frequency and is manifested by anemia, jaundice, spherocytes (ballooned erythrocytes), increase of reticulocytes, diminished resistance of erythrocytes to hypotonic saline, indirect van den Bergh, urobilinogen in the urine and splenomegaly. The disease is characterized by incomplete remissions and exacerbations. At any time, there may occur a hemolytic crisis manifested by fever, lassitude, abdominal pain, vomiting, dyspnea and palpitation. The crisis may be severe enough to cause death. *Pathologically*, the spleen is enlarged to as much as 1500 gm. The capsule is smooth, the edges are rounded, the consistency is smooth, and the cut surfaces are deep red and bulging. *Histologically*, there are diminution in size and number of lymphoid follicles, engorgement of the pulp and dilatation of the sinuses. The disease is cured by *splenectomy*.

Primary Thrombocytopenic Purpura—Primary thrombocytopenic purpura or essential purpura hemorrhagica is to be differentiated from purpura secondary to blood diseases, infection, intoxication, etc. Its precise *cause* is not known, although several theories hold (1) that reticulo-endothelial phagocytosis of platelets by the spleen is all important, (2) that the spleen is responsible for a substance which acts on the bone marrow, megakaryocytes and blood platelets, (3) that there is a faulty maturation of megakaryocytes and (4) that not only are the platelets at fault but that there is a disturbed function of the capillary walls. The disorder is characterized by bleeding from mucosal surfaces and hemorrhages into the skin and internal organs. There are a reduction of circulating blood platelets, anemia, normal bleeding time, normal clotting time, but an absence or delay of clot retraction, reticulocytosis, normal or moderate increase of circulating leukocytes, normal or slight hyperplasia of marrow cells by sternal puncture and a positive tourniquet test. The disease is characterized by exacerbations and remissions that last a few months or many years. *Treatment* is medical, but if this fails splenectomy is specific. The spleen is normal in size or slightly enlarged. Phagocytosis of platelets is said to be demonstrable by supravital staining. *Histologically*, however, the spleen appears normal or shows only moderate reticulum cell hyperplasia.

Banti's Syndrome—This has already been referred to under portal hypertension. The disorder is characterized by splenomegaly, non-hemolytic anemia, leukopenia, thrombocytopenia, development of collateral circulation between the portal and systemic circulations, repeated hematemesis, ascites and often cirrhosis of the liver. The weight of evidence appears to point to obstruction to the portal circulation as the cause of the disorder and, therefore, the synonym "congestive splenomegaly" seems appropriate. One essential, however, is that the venous pressure in the systemic system is normal.

Metastases to the liver, lymph nodes, lungs and bone marrow are common. *Treatment* is splenectomy. The *prognosis* is poor.

Secondary Tumors.—These tumors of the spleen are reported as occurring in from 0.3 to 4.8 per cent of all persons with cancer coming to necropsy. This relative *immunity* is said to be the result of (1) a paucity of lymphatics in the capsule and trabecles and their absence in the pulp, (2) constant contractions of the spleen and (3) an inherent or acquired antipathy of the spleen towards neoplastic growths. The neoplasm affects the spleen by blood stream metastasis, contiguity or generalized abdominal seeding. The primary site of the tumor has been found in all organs and tissues of the body, with carcinoma of the stomach and lungs leading the list. The spleen may or may not be enlarged, and the tumors both grossly and microscopically are similar to metastatic growths in other organs.

Mechanical Disturbances.—Under this heading will be included rupture of the spleen, hemolytic jaundice, primary thrombocytopenic purpura, Banti's syndrome, primary splenic neutropenia and panhematopenia, Fetty's syndrome, thalassemia and indications for splenectomy.

Rupture of the Spleen.—This is relatively common. It occurs at all ages. Frequently, there is a history of *trauma* such as a fall, kick, blow, penetrating wound, automobile accident and the like. At other times, there is no apparent cause and the injury then is said to be due to movement of the spleen, particularly in the presence of adhesions, to pressure of adjacent viscera or to increased intra-abdominal pressure consequent to coughing, straining and sneezing. In rare instances, the spleen in these cases of "*spontaneous*" rupture is normal but more frequently it is the seat of a pathologic process. Some of the latter are infectious mononucleosis, malaria, leukemia, typhoid fever, septic spleen, Banti's syndrome, neoplasm and adhesions. In the absence of massive hemorrhage, there is only sudden and severe or mild left upper quadrant pain that often radiates to the left shoulder. In the presence of acute hemorrhage, there are pallor, shock, anxious facies, drop in blood pressure and erythrocyte count and leukocytosis to 18,000 per cubic millimeter. There are tenderness and muscle spasm over the splenic area. *Pathologically*, there may be fragmentation of the spleen, detachment of the pedicle, numerous deep lacerations or a single rent, small peripheral tears that may be plugged by hematomas or omentum and subcapsular hemorrhage. The latter two may be silent for from twenty-four hours to two weeks or more, at which time massive hemorrhage may occur. This is called "delayed" rupture. *Treatment* is immediate splenectomy. Seeding of splenic tissue throughout the peritoneum may eventuate in autotransplants—a condition known as *splenosis*. The postoperative mortality rate reaches as high as 20 per cent. Without removal of the spleen, the death rate in more extensive lacerations is 100 per cent. There is, however, no way of telling how many smaller tears seal spontaneously.

Hemolytic Jaundice.—This is usually divided into congenital and *acquired*. The latter may be secondary to infection and other

The course is steadfastly progressive. The disease will not respond to iron or liver therapy, is benefited by transfusions and is temporarily aided by splenectomy. Death usually results from secondary infection. The spleen is greatly enlarged, covered with adhesions and may show infarcts. *Histologically*, there are fibrosis, extramedullary hemopoiesis and collections of large foam cells. The bone marrow is hyperplastic and discloses immature cells.

Indications for Splenectomy—These indications may be divided into conditions in which the procedure is *curative* or mandatory, and conditions in which it is of temporary or *equivocal value*. The latter includes Felty's syndrome, thalassemia and Gaucher's disease. The former consists of hemolytic jaundice, primary thrombocytopenic purpura, Banti's syndrome, primary splenic neutropenia and panhematopenia, "primary" abscess, "primary" fibrocystic tuberculosis, primary benign and malignant tumors, rupture and torsion.

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so that there is a reversal of the normal flow of blood. *Grossly*, the spleen is enlarged to as much as 5000 gm. The capsule is thick, fibrotic and adherent to adjacent structures. The organ is firm and on section discloses a homogeneously greyish red or salmon pink parenchyma. *Histologically*, there are small lymphoid follicles, distinct trabecles, dilated and conspicuous sinusoids, reticulum hyperplasia and fibrosis of intersinusoidal tissue, and hemorrhages in the pulp, trabecles and around arterioles. In time, many of these form siderotic nodules. They consist of yellow, brown, green or black granular pigmentations that are deposited along connective tissue and elastic fibers, and are composed of encrustments of iron and calcium. The only effective *treatment* in Banti's syndrome is splenectomy and in cirrhosis or hilar block, anastomosis of the splenic vein to the renal vein, or of the portal vein to the inferior vena cava. Splenectomy cures only when the obstruction is in the splenic vein.

Primary Splenic Neutropenia and Panhematopenia.—These are congenital disorders in which there is excessive destruction by the spleen of neutrophils and of all the normal circulating blood elements respectively. They are accompanied by fatigability, weakness, nervousness and a susceptibility to intercurrent infections. *Pathologically*, there are no characteristic findings in the spleen, but supravital staining is said to disclose excessive phagocytosis by the reticuloendothelial cells. *Treatment* is splenectomy. The *results* are good.

Felty's Syndrome.—This syndrome consists of atrophic arthritis, splenomegaly, normochromic anemia, leukopenia and loss of weight. It is attended by fever, fatigue, weakness, brown pigmentation of exposed skin, lymphadenopathy or hepatomegaly. It should be added, however, that some observers doubt the existence of the syndrome and contend that the changes mentioned are merely general manifestations of any atrophic arthritis. The *spleen* is usually from two to four times the normal size and histologically, shows only a diffuse fibrosis, dilatations of the sinuses and indistinct trabecles and lymphoid follicles. Splenectomy, while advocated, is not always curative.

Thalassemia.—This is also *known as* Mediterranean anemia, Cooley's erythroblastic anemia or simply Cooley's anemia. It represents an inherited abnormality of erythrocytes and exists in two forms (1) *thalassemia major*—more serious and found in offsprings who inherit the anomaly from both parents and (2) *thalassemia minor*—less serious, usually unaccompanied by symptoms and found in offspring who inherit the anomaly from only one parent (the other parent being normal). The disease is encountered in descendants of Mediterranean countries. In *thalassemia major* there is an insidious onset of anemia, pallor, splenomegaly of a size filling most of the abdomen, fever, weakness, stunting of growth, mongoloid facies, cardiac decompensation, anasarca, thinning of the cortices and expansions of the medullas of the bones, and a characteristic hemogram. The latter discloses hypochromic microcytic anemia, washed out or target erythrocytes, normoblasts, leukocytosis to over 50,000 per cubic millimeter and immature myeloid cells.

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portion of the urethra in the male give rise to the *prostate*, whereas in the female they result in the *paraurethral glands of Skene*. Buds from the cavernous portion of the urethra in the male result in the *bulbourethral glands of Cowper*, whereas in the female the homologues are the *vestibular glands of Bartholin*.

URETHRA

ANATOMY

The *male urethra* is about 20 cm long. It consists of three parts: (1) *Prostatic*. This measures about 4 cm in length and runs through the anterior portion of the prostate. Along the floor there is a urethral crest (*verumontanum*). Lateral to this are prostatic sinuses into which open the prostatic ducts. The distal end of the crest contains the *utricle (cul-de-sac)* which is the homologue of the *vagina* and on each side of this is the opening of an ejaculatory duct. (2) *Membranous*. Except for the external orifice this is the narrowest part of the urethra. It perforates the urogenital diaphragm, is surrounded by a sphincter muscle and measures about 2 cm in length. (3) *Cavernous*. This forms the rest of the urethra. It has a posterior dilatation (the *bulb*) and an anterior one in the glands (the *fossa navicularis*). It contains numerous glands (*Littre*) and ends in the external meatus. The *female urethra* is about 4 cm long. It starts in the urethral orifice of the bladder, pierces the urogenital diaphragm and empties in front of the opening of the *vagina* at the base of the *clitoris*. The lymphatics of the urethra drain into the deep subinguinal, hypogastric, external iliac and common iliac nodes.

Histologically, the *male urethra* in its prostatic portion is lined by transitional epithelium, in its membranous and proximal cavernous portion by stratified or pseudostratified columnar epithelium and in its distal cavernous portion by stratified squamous epithelium. Goblet cells are found scattered throughout the mucosa and the epithelium dips into the tunica propria to form the glands of *Littre*. The tunica propria is composed of elastic fibers, connective tissue and bundles of smooth muscles. The *female urethra* is lined by stratified squamous epithelium with varying amounts of pseudostratified columnar epithelium added. This dips into the tunica propria to form glands that are analogous to the peri-urethral and prostatic glands in the male. Beyond the tunica propria there is smooth muscle, and this distally is strengthened by striated muscle.

PATHOLOGY

Congenital Anomalies—Developmental abnormalities of the urethra consist of the following: (1) *Hypospadias*—opening of the urethra ventrally at any point between its normal position in the glans and the perineum. Its most common exit is at the level of the corona. (2) *Epispadias*—opening of the urethra along the

Chapter XVII

URINARY SYSTEM

EMBRYOLOGY

THE urinary system arises in conjunction with the genital system from condensed mesoderm known as the urogenital ridge. The kidney develops in three successive and overlapping stages. The first kidney or *pronephros* consists of a series of secreting tubules. One end of each tubule opens into the celom and the other end empties into an excretory or pronephric duct which enters the cloaca. Glomeruli, composed of arterial tufts, are separate. The *mesonephros* or Wolffian body constitutes the second kidney. The tubules are more complicated. One end drains into the retained pronephric duct which is now known as the mesonephric or Wolffian duct, and the other end is indented by the glomerulus. The *metanephros* is the third or permanent kidney. It is composed of glomeruli, Bowman's capsules and secretory tubules which are derived from the mesenchyme (nephrogenic cord) and collecting tubules, calyces, renal pelvis and ureter which develop from a ureteric bud that arises from the mesonephric duct. Initially, the collecting tubules form four buds from the renal pelvis and grouping of mesenchyme about these results in the formation of lobules. Later, the tubules still aggregate to form masses called pyramids, and these constitute the medulla of the kidney. The parenchyma that caps the pyramids forms the cortex, and prolongations of the cortex between the pyramids form the renal columns of Bertin. The original secreting tubules of the metanephros disappear and are replaced by permanent ones that develop from the mesenchyme. The lower portion of the urinary tract arises from the *cloaca*. This is a blind caudal expansion of the hind gut which is connected ventrally with the allantoic stalk, laterally with the mesonephric ducts and posteriorly with the future rectum. A coalescence of lateral ridges in the cloaca and a down growth of mesenchyme from above (which is known as the urorectal septum) separate the *bladder* and urogenital sinus anteriorly from the rectum posteriorly. With growth, the openings of the mesonephric ducts are shifted caudally to empty into an elevation known as Muller's tubercle. (In the male this forms the *colliculus seminalis*.) The ureteral openings are at the same time detached from those of the mesonephric ducts and are pushed more laterally. The bladder expands to form an epithelial sac that tapers superiorly to form the *urachus*. The latter connects with the allantois and with descent of the bladder is drawn caudally. In the female, the *urethra* is formed from the short neck between the bladder and urogenital sinus, whereas the upper part of the urogenital sinus (pelvic portion) and the lower (phallic) portion form the vestibule. In the male, the urogenital sinus forms practically all of the urethra. Buds from the posterior

in the discharging pus. From a few days to two weeks after contact the patient experiences burning on micturition and examination discloses pus at the meatus. Within the next few days the opening becomes red, everted and glued together with exudate. The latter at first rather thin and grey soon becomes copious thick and creamy. The urethral mucosa participates in a similar reaction for the organisms multiply in the fossa navicularis and peri-urethral glands, whence they extend between the epithelial cells and sometimes involve the peri-urethral tissue. In about one fifth of all cases, the inflammation resolves spontaneously in from five to six weeks. In the rest, however, the infection spreads or persists and may result in any of the following *complications*, inflammation or abscess of the peri-urethral tissue, prostate, seminal vesicles and epididymides, septicemia, pyemia, endocarditis, arthritis and fibrous strictures of urethra. The latter are usually multiple and are prone to occur in the anterior and bulbomembranous portions. The *diagnosis* of gonorrhea is established by demonstrating the organisms within neutrophils, by culturing them on special media and by a positive complement fixation reaction. *Treatment* consists of administration of one of the sulfonamides or of an antibiotic (currently penicillin). The *prognosis* in patients thus treated is excellent.

Reiter's Disease—This is mentioned because it simulates rather closely some cases of gonorrheal infection. It is said, among other agents, to be caused by a pleuro-pneumonia like organism or a virus. The disorder is characterized by an initial diarrhea and this is followed by urethritis, conjunctivitis and migratory arthritis. It is seen only in men between the ages of sixteen to forty-five years, has nothing to do with sexual contact and terminates spontaneously in from two to four months.

Tumors—Neoplasms of the urethra may be classified as follows from the epithelium, a papilloma and carcinoma, from connective tissue, a fibroma, fibrosarcoma and myxosarcoma, from muscle, a myoma, from connective tissue and muscle, a fibromyoma, from reticulum cells, a lymphosarcoma, from melanoblasts, a melanoblastoma, and, finally, a heterogeneous group of tumors known as caruncle. The only three that are frequent enough to be considered further are papilloma, caruncle and carcinoma.

Papilloma—Papillomas of the urethra may be villous like those of the urinary bladder or they may be sessile, warty and covered with stratified squamous epithelium. The former usually occur in the posterior urethra and the latter in the anterior urethra. Although they are true tumors, they probably originate on an infective basis. *Symptoms* consist of irritation, frequency of micturition and spontaneous hemorrhage or hematuria. Anterior growths can usually be seen by direct inspection of the urethra, while posterior tumors are visualized with the aid of the urethroscope. *Treatment* is diathermic coagulation.

Caruncle—This is a benign, crescentic, polypoid growth of the distal portion of the female urethra. It usually arises in the floor and is located just within the meatal opening. Ordinarily, the mass is not more than 6 mm. in diameter. It is raised, irregular, sessile,

dorsum of the penis. This anomaly is rare. (3) *Fistula* between the rectum and urethra. (4) *Reduplication* of the urethra—one of the rarest abnormalities. This may be complete and extend from the bladder to the glans, but more commonly it is blind proximally, opens onto the glans and is located dorsal or ventral to the main urethra. In still other cases, the distal end of the accessory urethra opens in or near the glans or at the penoscrotal junction, and the other end joins the main urethra more proximally. (5) *Stenosis*. This may be congenital, in which case it occurs most commonly at the external meatus, or it may be acquired. The latter results from trauma such as indwelling catheter, instrumentation and rupture of urethra or from inflammation particularly that following gonococcus infection. The result of urethral stenosis is urinary retention with dilatation of the bladder, ureterectasis and hydronephrosis. There are dysuria, frequency, hematuria and, in children, enuresis. (6) *Atresia*. This can occur along the entire course in which case there is no urethra or it may be segmental. The most common sites of the latter are at the meatus and the membranous portion. (7) *Diverticula*. These are congenital or acquired. The former are rare, while the latter are frequent. Acquired diverticula result from trauma which weakens the wall, from obstruction to the outflow of urine with ballooning of the proximal segment and from infection of a peri-urethral gland with formation of an abscess and establishment of a secondary communication with the urethra. (8) *Hypertrophy* of the *verumontanum*, enough to cause urinary obstruction. (9) *Congenital valves*. These occur at the verumontanum and consist of two leaf-like affairs that extend from the verumontanum to the lateral wall of the urethra above or below the point of origin, or the valve is of the iris type and partially or completely encircles the urethra. The clinical and pathologic manifestations are the same as those with urethral stenosis.

Inflammations.—Inflammation of the urethra is known as urethritis. It may be non-specific and acute or chronic, or it may be specific and granulomatous. The latter are not common. *Tuberculosis* usually starts in the posterior portion of the cavernous urethra and exists as raised granular yellowish grey tubercles, as caseating nodules or as punched out and undermined ulcers. It is usually associated with tuberculosis of the upper portion of the urinary tract. *Syphilis* exists in the form of a primary sore or mucous patches. *Acute urethritis* may be caused by staphylococci, streptococci, pneumococci, colon bacilli, micrococcus catarrhalis, trichomonas vaginales, gonococci and many other bacteria. *Chronic urethritis* frequently follows acute urethritis and can be caused by any of the aforementioned organisms. At other times, the process is chronic from the start and originates as a result of trauma such as indwelling catheter, instrumentation, rupture of the urethra, etc. or as a result of urethral obstruction.

Gonococcal Urethritis.—This is the most important acute infection. It is usually acquired by sexual intercourse and is caused by the *Neisseria gonorrhoeae*—a gram negative, bean-shaped diplococcus which is characteristically found within neutrophils that are present

tables such as peas and beans. The complications are obstruction to the outflow of urine and perineurithal inflammation.

Trauma to the urethra may be (1) *internal* from instrumentation, foreign bodies or stones and usually results in lacerations. In addition, chemical burns caused by iodine, silver nitrate and mercury bichloride are not uncommon, and (2) *external* is a result of falls, kicks or blows. This usually results in complete or incomplete rupture. On rare occasions, the female urethra is ruptured during intercourse. The bulbous urethra is commonly injured by straddling falls, while the membranous urethra is frequently injured in fractures of the pubic bones. The clinical manifestations may consist of ecchymosis, swelling, hematuria, pain, urinary retention and extravasation of urine. *Treatment* consists of re-establishing the continuity of the canal.

Calculi in the urethra may be secondary from the higher urinary passages or they may be primary. In the latter instance, they practically always arise behind strictures or in diverticuli. Migrating urethral stones are often accompanied by sharp pain, hematuria, dysuria or acute retention, while stationary urethral stones may cause ulceration, abscess and fistula. Treatment consists of removal by one means or another.

Obstruction to the urethra may be caused by (1) congenital lesions, such as stenosis, atresia, hypertrophy of verumontanum and valves, (2) inflammations, particularly the fibrosis that results from severe gonorrhea, (3) neoplasms and (4) mechanical factors, such as direct trauma, foreign bodies and calculi.

BLADDER

ANATOMY

The bladder is a sac that normally varies in size from a capacity of 120 to 320 cc. When it is distended, it is ovoid and ascends above the level of the pelvic brim, but when it is contracted, it is somewhat pyramidal and intrapelvic. In the latter state, it consists of the following: (1) A *base* that is separated from the rectum by the seminal vesicles and vas deferens in the male, and the uterus and upper part of the vagina in the female. (2) *Apex* which is located superiorly and gives attachment to the urachus or middle umbilical ligament. (3) *Superior surface* that is in contact with the pelvic colon and coils of the small intestine. (4) *Lateral borders*. (5) *Inferior surface* which is separated from the pubis by the retropubic pad of fat, and in the male rests against the prostate. About the bladder, there are a series of *ligaments*, the most important of which are the lateral and anterior *true ligaments* which connect the organ with the pubic bones. The *mucosa* is loosely attached and wrinkled, except at the base over the trigone where it is firmly bound and smooth. The *trigone* is a triangular area formed by the urethra and ureters. Each of the sides of the triangle measure 2.5 cm. in length when the bladder is contracted, and as many as 5 cm. when it is distended. The ureteral orifices are normally slit-like. The *arterial*

grey or hemorrhagic, often superficially ulcerated and frequently exquisitely tender to touch. *Histologically*, the surface is covered with stratified squamous epithelium which may dip into the underlying tissue to form solid nests and cords. The core is composed of (1) loose or dense connective tissue in which there are numerous engorged capillaries or cavernous spaces, or (2) a mass of granulation tissue. This consists of a background of fibroblasts and connective tissue and a diffuse infiltration with plasma cells, lymphocytes, monocytes and neutrophils. A cancerous transformation rarely occurs. *Clinically*, aside from the exquisite tenderness, they are responsible for pain and burning on urination. Caruncles can be differentiated from carcinoma with certainty only by histologic study. *Treatment* is excision or destruction with electrocautery. If not completely destroyed, the lesion may recur.

Carcinoma.—This tumor is more frequent in the urethra of females than of males. The precise *cause* as in other carcinomas is not known, but it is thought that previous diseases in the form of trauma, inflammation, stricture and leukoplakia play an active rôle. The disease predominates in the latter part of the fifth and the beginning of the sixth decades of life. *Clinical* manifestations are not pathognomonic and consist of dysuria, frequency, diminution in size of the stream, occasionally hematuria and sometimes the presence of a tumor. The growth may be located in any portion of the urethra and it exists in one of three *forms*, (1) fungating papillary or cauliflower-like, (2) annular constricting and infiltrating and (3) an indurated ulcer with everted hard edges. *Histologically*, most of the cancers are of the squamous cells variety, but transitional cell carcinoma, adenocarcinoma and mucoid carcinoma have also been described. *Spread* is by contiguity to peri-urethral tissues in which case, because of accompanying ulceration, fistulous tracts and abscesses are common. The latter are particularly frequent at the penoscrotal junction in growths of the posterior male urethra. Spread also takes place by way of the lymphatics to the deep sub-inguinal, external iliac, hypogastric and common iliac nodes, and less often by way of the blood stream to the lungs and liver. If the tumor is located in the anterior portion of the urethra in the male, *treatment* is amputation of the penis. Tumors of the posterior portion of the male urethra and all tumors of the female urethra are treated by resection. In any case, the inguinal nodes should be removed by dissection. The *prognosis* depends largely upon the location of the cancer. It is fair if the growth is in the anterior portion of the male urethra but it is poor if the primary site is elsewhere.

Mechanical Disturbances.—These may be considered under (1) foreign bodies, (2) trauma, (3) calculi and (4) obstruction.

Foreign Bodies.—Foreign bodies in the urethra are less common than they are in the bladder, for usually the urethra serves only as a passage way. However, as a result of surgical accidents, sexual perversion or self-treatment many objects are arrested. As one would expect they are quite varied. Some of the more common ones are hair pins, hat pins, nails, pencils, fish bones, hair and vege-

pubic bones and the anterior wall of the bladder. Consequently, the ureters open directly onto the surface, the urethra is absent and the penis is flat dorsally. Associated malformations are cryptorchidism, bifid scrotum, cleft clitoris, rudimentary labia and intestinal fistula. Because the urine empties externally there is usually marked local excoriation, infection and ulceration and occasionally, neoplastic transformation. If the condition is not corrected, death, as a rule, results from ascending pyelonephritis and renal failure, (7) *urachal abnormalities*. These may be listed as (a) failure to form in which case the bladder does not descend, (b) failure to descend resulting in a fetal type of bladder, (c) deviation from the midline, (d) segmental occlusions resulting in cysts, (e) failure of obliteration of the upper end resulting in a vesico-umbilical fistula and (f) laceration or rupture if attachment is firm and descent is rapid.

Inflammations—Inflammatory lesions of the bladder may be divided into (1) non-specific which include acute cystitis, gangrenous cystitis, proliferative cystitis, chronic interstitial cystitis and incrustated cystitis and (2) specific or granulomatous infections which include tuberculosis, malakoplakia, blastomycosis, actinomycosis, schistosomiasis and syphilis.

Acute cystitis is usually caused by the colon bacilli, staphylococci, streptococci, pneumococci and bacillus proteus. The organisms gain entrance (1) by way of the urethra either spontaneously or as a result of catheterization or instrumentation, (2) from the kidneys, particularly in the presence of urinary obstruction, (3) by contiguity from adjacent organs and (4), rarely, by direct external trauma. **Symptoms** consist of urgency of micturition, frequency, dysuria, pyuria and, rarely, a systemic reaction. The gross changes vary according to the severity of infection. The most frequent site is the trigone, but any portion or all of the mucosa may be involved. There are congestion, edema, exudation, ulceration, ecchymoses and granulating elevations. **Histologically**, the mucosa may be edematous, thickened, attenuated or ulcerated. The tunica propria is neutrophils, plasma cells, lymphocytes and monocytes. The inflammation extends along the connective tissue septa between the muscle bundles. **Treatment** consists of removal of the cause of the infection and the administration of sulfonamides and antibiotics.

Gangrenous cystitis may be localized or generalized. The former is more frequent in women as a result of pressure by a pregnant uterus. The latter is more common in men, is usually a terminal event and results from vascular occlusion (that ordinarily eventuates from internal or external pressure) in association with bacterial invasion. The lesion is serious for it is attended both by severe local and general symptoms. The mucosa is swollen, deep red to green or black, friable and irregularly sloughed, and the rest of the wall is thick because of edema and cellular infiltration. The mortality is high.

Proliferative cystitis is a term used to cover a group of lesions that arise as a result of chronic inflammation and are characterized by the presence of mucosal granularities or larger nodulations. Included are (1) *cystitis follicularis*—the presence of lymphoid folli-

supply is derived from the vesical arteries that arise from the anterior trunk of the hypogastric. The *veins* form a plexus that ends in the hypogastric veins. The *nerve* supply is derived from the sacral parasympathetics and from the hypogastric plexus. The *lymphatics* from the anterior portion drain into the external iliac nodes, and those from the posterior portion into the hypogastric, external and common iliac nodes.

Histologically, there are three coats—the mucosa, tunica propria and muscle (Fig. 337). The mucosa consists of transitional epithelium, the cells of which are 6 to 8 layers in depth. Gland-like structures arising in the mucosa and similar to the glands of Littre are found only near the urethral orifice. The lamina propria consists of elastic fibers and rather dense connective tissue superficially, and loose connective tissue in its deeper portion. The muscle is of the smooth variety and consists of an outer longitudinal, a well-developed intermediate spiral and a poorly developed inner oblique layer.

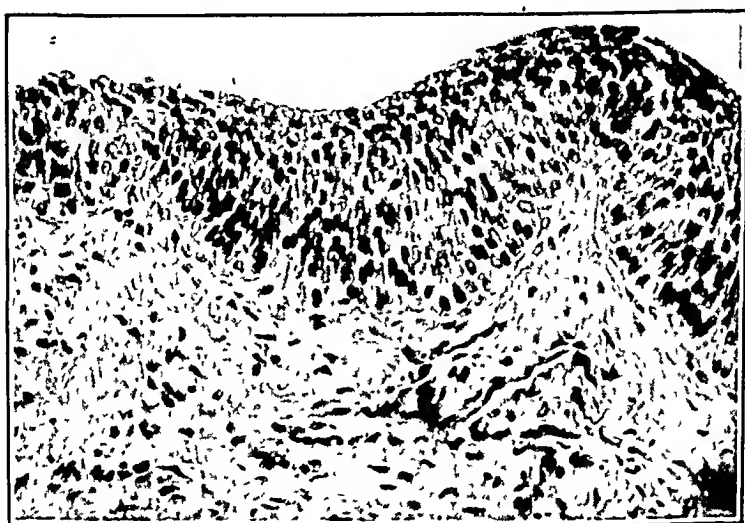


FIG. 337 —Normal bladder showing transitional epithelium and tunica propria. x 100.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the bladder consist of (1) *vesico-vaginal* and *vesico-rectal fistulas*, (2) complete *absence*, (3) *hourglass* deformity, (4) *double bladder* formed by septum which is complete or incomplete, (5) *diverticula*. These are congenital or acquired. The former are rare the latter are common and usually occur as a result of vesical neck obstruction. Most commonly, this is due to enlargement of the prostate. The diverticula are located in all areas, measure from less than 2 cm. to more than 10 cm. in diameter, are single or multiple, have large or small ostia, and are composed of an intact, attenuated or ulcerated mucosa and a thin fibrous tissue wall which contains varying amounts of muscle. Diverticula are prone to develop tumors, calculi, ureteral obstruction and infection; (6) *exstrophy*. This may be defined as an eversion of the bladder onto the anterior abdominal wall as a result of a deficiency in the anterior abdominal wall, the anterior

Blastomycosis and actinomycosis of the bladder are extremely rare infections. The latter is more often an extension from adjacent structures than it is primary. Histologically, the lesions resemble those described in the skin. **Schistosomiasis** of the bladder is caused by *schistosoma hematobium*—a blood fluke. The lesions are confluent papillary-like growths usually located around the trigone. They do not have a characteristic histologic appearance. The diagnosis is established by finding the ova in the urine or in microscopic sections.

Syphilis of the bladder is rare. It occurs both in the secondary and tertiary stages.

Tumors—Neoplasms or neoplastic-like conditions of the bladder may be classified histogenetically as follows: from epithelium leukoplakia (not a true tumor but considered by some as a premalignant condition), papilloma and carcinoma, from connective tissue, fibroma, myxoma, fibromyxoma, fibrosarcoma and myxosarcoma, from nerves, neurofibroma and neurosarcoma, from vessels, hemangioma, angiosarcoma and Kaposi's sarcoma, from fat, lipoma, from muscle, leiomyoma, leiomyosarcoma, rhabdomyosarcoma and myoblastic sarcoma, from lymphoid tissues, any of the lymphoblastomas including lymphosarcoma, Hodgkin's disease, reticulum cell sarcoma, plasmacytoma and the leukemias, from embryonal rests, dermoid and malignant mixed tumor or embryoma, from mesodermal elements as a result of metaplasia (probably from reticulum cells), osteoma, chondroma, osteogenic sarcoma and chondrosarcoma, and from extraneous sources, endometriosis and secondary tumors.

Sarcomas of the urinary bladder have certain common characteristics. They occur at all ages but reach a peak in the first and fifth decades of life and affect males twice as frequently as females. They are usually localized but may be multiple and diffuse, and they are frequently located at the trigone, around the ureteral orifice or the urachus. They grow as large bulky sessile or pedunculated masses that fill the vesical lumen or they simultaneously extend through the bladder wall. Metastasis is not common. The histological picture varies with the type of growth. Clinically, they result in dysuria, frequency and less often hematuria. The diagnosis is made by cystoscopy and biopsy. Treatment consists of total cystectomy. The prognosis is poor. Most patients die from obstructive urinary tract infection.

Secondary tumors of the bladder are more frequent than sarcomas but less frequent than primary carcinoma. For practical purposes, there are only four growths in this group, namely, carcinoma of the cervix, carcinoma of the rectum and sigmoid, carcinoma of the prostate and carcinoma of the ureter and renal pelvis. The latter two reach the bladder by implantation or in the case of low ureteral growths by direct extension, while the others practically always involve the bladder wall by contiguity.

Primary carcinoma of the urinary bladder is the most common and the most important of all tumors in this unit. Under this caption are also included papillomas, for their behavior justifies them

cles with germinal centers in the tunica propria, (2) *cystitis granulosa* and *polyposa*—clusters of protruded granulation tissue, (3) *cystitis glandularis*—the presence of gland-like structures in the tunica propria that are derived from the mucosa, (4) *cystitis cystica*—dilated gland-like spaces of similar origin and (5) *cystitis emphysematosa*—the presence of bacteria-produced gas-filled spaces in the tunica propria. Although any of the aforementioned may be present alone, there is usually a mixture of two or more in the same bladder and even in a single biopsy.

Chronic interstitial cystitis, also known as *Hunner's ulcer*, is an inflammation of the subepithelial and intermuscular connective tissue of the bladder. There are edema, increased vascularity and infiltration with lymphocytes, neutrophils, plasma cells, monocytes and erythrocytes. The mucosa is thinned and sometimes ulcerated. *Grossly*, the bladder is contracted; the wall is thickened, and the mucosal surface, when viewed with the aid of a cystoscope, shows irregular areas of salmon-pink discoloration. When the bladder is distended these areas crack and bleed. The *cause* of the lesion is unknown, but it is thought that the infection spreads to the bladder from inflammations of nearby structures.

Incrusted cystitis is a mucosal deposition of magnesium and ammonium phosphates derived from urea by the action of bacteria. The involved portions of the bladder are covered with densely adherent white calcific plaques and the uninvolved areas show advanced inflammation.

Tuberculosis of the bladder is almost always secondary to tuberculosis of the kidney. It occurs most often between the ages of twenty to fifty years and is more frequent in males. *Clinically*, there are frequency, dysuria, urgency and hematuria. The site of predilection is the trigone, but any part of the bladder may be affected. The initial *lesion* is found around the ureteral opening as an intense congestion. Shortly, tubercles appear and these are followed by ulcerations. The latter extend to the adjacent mucosa as irregular undermined shallow ulcers that are surrounded by intense hyperemia. The subjacent wall is rigid and unyielding; the rest of the mucosa is inflamed, and the bladder capacity is reduced to as little as an ounce. As the process advances, there is considerable fibrosis, and this renders the ureteral orifice stenotic and distorted or patulous. The *diagnosis* is established by isolating the tubercle bacilli from the urine. If the renal lesion is unilateral, nephrectomy cures the vesical disease. If the renal lesion is bilateral, *treatment* is symptomatic but unsatisfactory for most of the patients die.

Malakoplakia is a chronic granulomatous lesion that occurs mostly in women beyond the age of thirty years. The *cause* is unknown, although inclusion bodies have been found in monocytic cells in some cases and in others, the *histologic* picture closely resembles proliferative tuberculosis and Boeck's sarcoid. *Grossly*, the lesion consists of one or hundreds of greyish or brownish yellow raised plaques or polypoid excrescences with overhanging edges and surrounded by a zone of hyperemia.

layers thick and consists of closely approximated polygonal cells with a moderate amount of homogeneously eosinophilic cytoplasm, and round or, at the most, oval vesicular nuclei. Mitoses are present but not numerous. As the degree of malignancy increases, the epithelium becomes irregularly heaped up in some areas and the tips of the villi become adherent to each other. The individual cells tend to become less mature. They show irregularity in contour, a decreased or increased amount of cytoplasm and more bizarre more hyperchromatic nuclei. Simultaneously, the tunica propria and the muscle become infiltrated with cords and nests of irregular cells

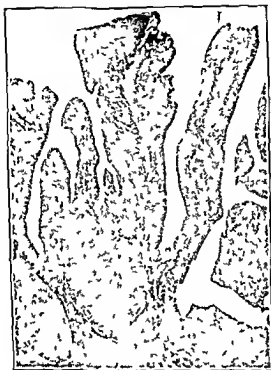


FIG. 339—Low grade papillary carcinoma of the urinary bladder $\times 370$

The degree of differentiation of the latter varies from (1) masses that still resemble transitional epithelium to (2) completely anaplastic small round or spindle shaped cells with condensed cytoplasm and pycnotic hyperchromatic nuclei or (3) large extremely bizarre and polyhedral cells with abundant cytoplasm and grotesque nuclei. The stroma may be well vascularized and scanty, it may be abundant cellular and almost sarcomatous-like, or it may be dense acellular hyalinized and copious. It contains varying degrees of plasma cell and lymphocytic infiltration. Aside from these histologic types, there occasionally arises as an infiltrating growth an ordinary squamous cell carcinoma and, as a fungating mass in the region of the urachus, an adenocarcinoma that is similar to an adenocarcinoma of the large bowel. Well-differentiated papillary growths remain confined to the mucosa for months and years, whereas in-

designation as carcinomas of low grade malignancy. The *causes* of vesical carcinomas are not known but chronic infection and a virus have been thought to be of etiological significance and, in selected cases, aniline dyes have been shown to precipitate their growth. Men are affected about six times as frequently as women, and the highest age incidence is between forty and seventy years. Early, the *symptoms* consist of hematuria, frequency, painful micturition, and urgency. Later, with extension of the growth, there is pain around the bladder, in the pelvis, about the rectum or over the renal areas.

Grossly, the tumors vary considerably. Most of them are situated at the base of the bladder, but they can involve any portion and are

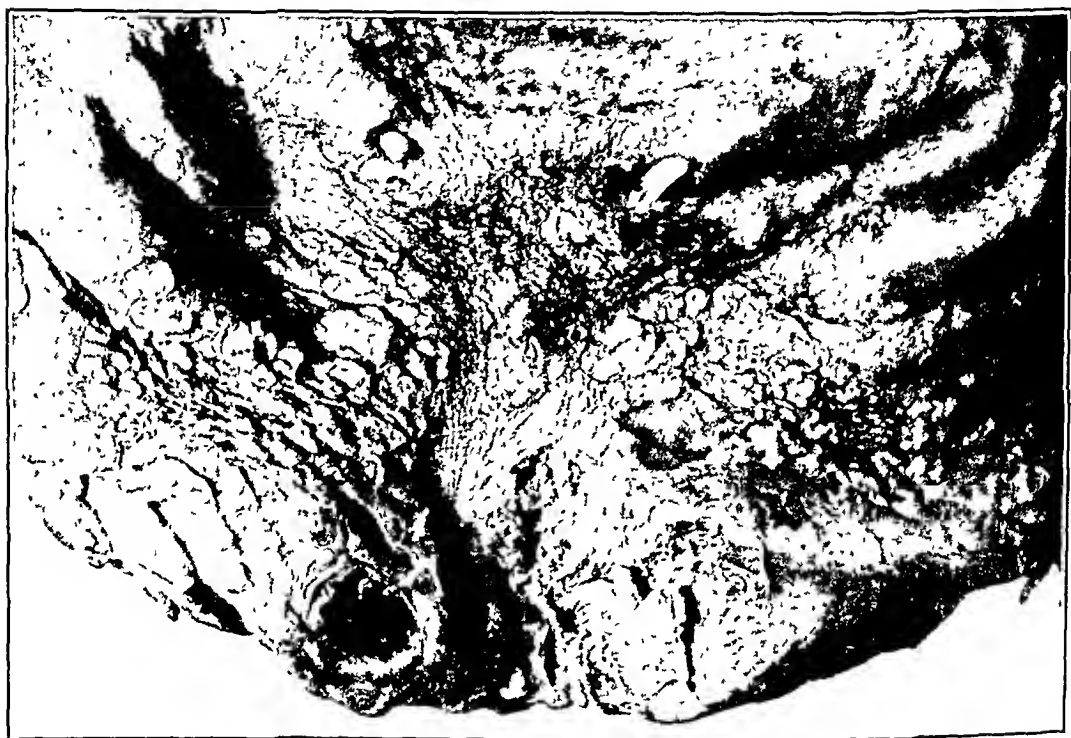


FIG 338.—Extensive papillary and infiltrating carcinoma of the trigone of the urinary bladder.

sometimes located in the region of the urachus (Fig. 338). They are single or multiple. The less malignant growths consist of pedunculated, slender, villous-like projections of friable, easily traumatized, pinkish-grey tissue. With increasing malignancy, the villi become glued, the growth becomes squattier, the pedicle becomes broader and the tumor infiltrates the adjacent bladder wall. In the highly malignant and undifferentiated neoplasms, the mucosal surface may be only slightly raised, granular or ulcerated and the entire growth may be found permeating between the muscle fibers. In such instances, the wall is thick, grey, indurated and unyielding. *Histologically*, the least malignant lesions or the so-called papillomas consist of delicate thin stalks of well-vascularized connective tissue covered with transitional epithelium that deviates but little from that of normal bladder mucosa (Fig. 339). It is as many as six

URETERS AND PELVES

ANATOMY

Each *ureter* measures about 30 cm in length, connects the renal pelvis with the bladder, is retroperitoneal, and consists of an abdominal and pelvic portion. The *abdominal portion* lies medial to the psoas major muscle, is crossed by the gonadal vessels and overlies the common iliac vessels. In addition, the right ureter is covered by the duodenum, right colic and ilio-colic vessels, mesentery and lower part of the ileum and the left ureter is crossed by the left colic vessels and the pelvic colon. The *pelvic portion* traverses the lateral border of the pelvic cavity, crosses the hypogastric artery then turns medially, and in the male, runs anterior to the upper part of the seminal vesicle before it enters the base of the bladder. In the female, the terminal portion is directed beneath the broad ligament, posterior to the uterine artery, lateral to the cervix and vagina, and finally anterior to the vagina to enter the base of the bladder.

Each *renal pelvis* is a funnel-shaped continuation of the corresponding ureter that enters the hilum of the kidney. It lies posterior to the renal artery which in turn is posterior to the renal vein. Towards the renal side, the pelvis breaks up into 2 or 3 major calyces which in turn divide into several minor calyces. The latter expand and are perforated by the collecting tubules.

Histologically, the pelves and ureters are similar to the urinary bladder. They consist of a mucosa of transitional epithelium, a tunica propria of connective tissue and a musculature composed of an inner longitudinal and an outer circular layer of smooth muscle with an additional longitudinal layer added in the lower third of the ureter.

PATHOLOGY

Congenital Anomalies—Developmental abnormalities of the pelvis and ureter are said to occur in 3 per cent of the population. Those of the pelvis consist of variations in number, size and shape of the major and minor calyces and of doubling or rarely triplication of the pelvis. Anomalies of the ureter may be listed as follows:

(1) Variations in number—2 to 5 on each side but usually 2 and the duplication may be complete or partial. The latter is more common in the upper part in which case the ectopic ureter usually joins the normal one, although it may end blindly. A blindly ending ureter may also arise from below. The terminal portions of complete accessory ureters empty into the bladder, or in the male, into the urethra, ejaculatory ducts, seminal vesicles or vas deferens and in the female, into the vestibule, vagina or uterus. (2) Dilatation. (3) Stenosis. (4) Atresia. (5) Entire absence. (6) Post caval. (7) Diverticula. (8) Valves of the mucosa. (9) Pinpoint uretero-pelvic junctions. (10) Kinks or spiral twists. (11) Ureterocele (congenital atresia of the lower end with prolapse of the mucosa and

filtrating tumors obstruct the ureters, *spread* through the wall to adjoining structures, creep along the nerve sheaths and permeate lymphatics and blood vessels. They thus metastasize to regional lymph nodes, liver, lungs, vertebrae and other areas.

Carcinoma of the urinary bladder should be suspected in any patient beyond the age of forty years presenting hematuria or symptoms of bladder irritability. The *diagnosis* is established by cystoscopy and biopsy. *Treatment* is not standardized and frequently leaves much to be desired. It consists of local transurethral destruction of the tumor, segmental resection, total cystectomy with transplantation of the ureters into the large bowel, or irradiation. The *prognosis* is best in well-differentiated papillary tumors and rapidly diminishes with increasing anaplasia. In the latter, the five year survival rate is less than 15 per cent.

Mechanical Disturbances.—Under this heading are included the following: (1) *Perforation*. This can occur as a result of (a) penetration by stabbing, bullets, shrapnel, splinters of wood, glass, spicules of bone from a fractured pelvis and instrumentation such as transurethral prostatic resection, cystoscopy and fulguration. In penetrating wounds, the bladder may be full or empty and the perforation may be intraperitoneal or extraperitoneal; and (b) rupture which results from sudden pressure upon a distended bladder and is usually extraperitoneal. The external force is usually a fall, kick or blow. Occasionally, the perforation is said to be spontaneous, but since this occurs in overdistended bladders, minor trauma cannot be ruled out. (2) *Obstruction*. This eventuates from lesions of the vesical neck which may be listed as (a) congenital—valves in the posterior urethra and hypertrophy of the verumontanum, (b) inflammatory—of posterior urethral glands in the female and the prostate in males, (c) tumors—of the bladder, prostate and extravesicular originating in the uterus, cervix and bones of the pelvis and (d) mechanical—foreign bodies, calculi and neurogenic disturbances. (3) *Hernia*. Herniation of the bladder into the vagina (known as cystocele) is common in women who have borne children. Aside from this, portions of bladder may be found in conjunction with inguinal and femoral hernias and, rarely, in association with perineal, sciatic, obturator and ventral hernias. (4) *Fistulas*. These are found between the bladder and vagina, rectum, adjacent skin or umbilicus and may be (a) congenital—vesico-vaginal, vesico-rectal and patent urachus, (b) inflammatory—prostatic abscess, peri-anal abscess, ischio-rectal abscess, regional enteritis and tuberculosis, (c) neoplastic—carcinoma of the prostate bladder, rectum and ovary, and (d) mechanical—external trauma, instrumentation, surgical accidents, pressure necrosis at the time of delivery and following irradiation. (5) *Foreign bodies*. These include calculi and, in addition to others, the objects that have already been enumerated in the section of the urethra.

URETERS AND PELVES

ANATOMY

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PATHOLOGY

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ballooning of the terminal segment). (12) Aberrant renal vessels or adhesive bands crossing at the uretero-pelvic junction and producing obstruction.

Inflammations.—Inflammatory lesions of the ureter and pelvis are quite similar to those of the urinary bladder.

Acute and chronic non-specific infections are relatively common and usually arise as a result of distal urinary tract obstruction. The *causative organisms* are many with colon bacilli, cocci and bacillus proteus predominating. The exact *route* of infection is still debatable. Three possible avenues are (1) ascension along the lumen, (2) ascension along the lymphatics and (3) excretion of organisms in the urine by the kidney. Because of stagnation of urine, the pelves and ureters are not cleansed, their resistance is lowered and the organisms gain a foot-hold. Less often, the ureters are secondarily involved from infection in adjacent tissues and organs. In *acute stages*, the walls are thickened and edematous; the mucosa is hyperemic, ulcerated and covered with an exudate; the lumen is dilated, and the ureter is elongated and tortuous. *Histologically*, these changes are confirmed with, in addition, a diffuse infiltration with neutrophils and lesser numbers of eosinophils, lymphocytes and plasma cells. In the *chronic stages*, the wall is thick grey and fibrotic; the tortuosity is less; the lumen is irregularly contracted or completely stenotic and contains pus, and the mucosa is completely denuded or regenerated and leukoplakic. *Histologically*, the dominant change is fibrosis with varying degrees of inflammatory cell infiltration. It should be added that infection of the pelvis (pyelitis) and ureter (ureteritis) are practically always accompanied by a similar process in the kidney itself.

Proliferative pyelitis and ureteritis (with the protean nomenclature listed under proliferative cystitis) are duplicated in the upper urinary tract and usually accompany the vesical infection.

Of the *granulomatous* infections, *tuberculosis* is the only lesion of any consequence. It is practically always secondary to renal disease. The pelvis becomes affected after the parenchymal infection becomes caseous and, when this occurs, the ureter is almost certain to become involved. In advanced cases the wall of the ureter is thick, rigid, and indurated; the mucosa is ulcerated, and the lumen contains multiple strictures between which it is filled with caseous material. In such cases the pelvis becomes dilated and the kidney is reduced in substance. In some instances, however, the ureters escape gross damage and the lesion is discovered only microscopically.

Tumors.—Neoplasms of the pelvis and ureter are uncommon. Although the structure of these organs is similar to that of the bladder, *primary* neoplasms that arise therein are not as varied. In each, there have been described from the epithelium, a papilloma and carcinoma; from connective tissue, a fibroma and fibrosarcoma, and from muscle, a leiomyoma and leiomyosarcoma. In addition, the pelvis is rarely the site of a primary hemangioma. *Secondary* tumors too are rare and usually occur as direct extensions from adjacent organs and tissues. Carcinoma of the kidney is the most

common tumor that involves the pelvis, while carcinoma of the bladder and cervix of the uterus are the chief ones that affect the meter.

Carcinomas of the pelvis and ureter comprise about 7 per cent of all cancers of the upper urinary tract. The cause is not known but leukoplakia, epithelial inclusions, mechanical or inflammatory irritation and excretion of "carcinogens" in the urine are considered to be significant. The tumor affects males three times as frequently as females and is most common in the sixth and seventh decades of life. The earliest symptom is hematuria which occurs in three quarters of all cases. Later, there are pain and tumefaction. The lesions grossly and microscopically are identical with those in the urinary bladder which have already been described. Any portion of the pelvis may be involved while the lower portion of the ureter is the favored site. The most common accompanying condition is hydronephrosis which occurs in three quarters of the cases. The cancer spreads by direct extension, perineural lymphatics, blood stream and implantation to involve the bladder, liver, vertebrae, kidneys, abdominal lymph nodes, pancreas, adrenals, lungs and other sites. The diagnosis is established by cystoscopy, ureterography and occasionally by demonstrating tumor cells in urinary sediment. The only effective treatment is nephrectomy and ureterectomy. Less than one third of the patients survive five years.

Mechanical Disturbances—These may be briefly listed under trauma and obstruction.

Trauma—Trauma to the pelvis and particularly the ureter may result from (1) external injuries such as stab wounds, gunshot wounds, tears and, less commonly, perforations by fractured fragments of the bony pelvis, (2) surgical procedures, such as perforation by catheters or stone extractors, ligation by ties particularly in operations on the uterus, crushing with clamps, lacerations in the process of freeing and perforations by needles, and (3) spontaneous rupture. This is extremely rare and can happen only when there is previous disease especially when this is associated with obstruction.

Obstruction—Obstruction to the ureter and pelvis may be caused by (1) congenital lesions, such as stenosis, atresia, mucosal valves, kinks, spiral twists, ureterocele, and aberrant vessels or fibrous bands crossing externally, (2) inflammations—non-specific or tuberculous, (3) neoplasms—primary within the ureter or secondary compression from without and (4) mechanical disturbances such as those listed under trauma above and, in addition, calculi.

KIDNEYS

ANATOMY

Each kidney measures about $12 \times 6 \times 3$ cm and weighs approximately 150 gm. It lies behind the peritoneum lateral to the twelfth dorsal and first three lumbar vertebrae. It is surrounded by fatty tissue, and this is enclosed by a fibrous sheath which is called the renal fascia. There are 2 surfaces, 2 borders and 2 poles. The

anterior surface is directed laterally and anteriorly. That of the right kidney is in contact with the adrenal, liver, duodenum and colon and that of the left kidney with the adrenal, stomach, spleen, pancreas, jejunum and colon. The *posterior surface* rests upon the diaphragm, lumbocostal arches, and psoas major and quadratus lumborum muscles. The *medial border* is concave and contains the hilum through which pass antero-posteriorly the renal vein, artery and pelvis. Immediately adjacent and loosely adherent to the kidney, there is a fibrous tissue investment that is lined by an incomplete layer of smooth muscle. On cut surface, the kidney presents an outer portion, the *cortex*, and an inner portion, the *medulla*. The latter exists in the form of pyramids between which the cortex is insinuated in small projections called renal columns (of Bertin).



FIG. 340.—Normal kidney showing glomerulus with its afferent arteriole, proximal convoluted tubules P, Henle's loop H and distal convoluted tubules D x 100.

The *arterial supply* is from the aorta, usually by way of a single vessel, but occasionally also by way of accessory polar arteries. The *veins* drain into the renal veins which empty into the inferior vena cava. The *lymphatics* join the upper aortic nodes. The *nerve supply* is from the celiac plexus and the tenth, eleventh, and twelfth thoracic nerves.

Histologically, the functional unit of the kidney is the nephron (Fig. 340). It consists of (1) a glomerulus—essentially a tuft of capillaries invaginating the upper portion of a tubule. It is surrounded by an outer membrane (Bowman's) which is entered by an afferent vessels and which is continuous with the second portion of the nephron, (2) the proximal convoluted tubule, (3) Henle's loop and (4) distal convoluted tubule. The latter is joined by a short tube with the collecting tubules which empties into the calyx. The tubules are lined with cuboidal epithelial that varies somewhat according to the level. The stroma of the kidney is composed of scanty connective tissue in which course veins, arteries and nerves.

PATHOLOGY

Congenital Anomalies—Developmental malformations of the kidney may be listed as follows (1) *Agenesis*—complete absence of renal parenchyma on one or both sides (2) *Aplasia*—defective formation The kidney is smaller than normal and composed of embryonic or calcified parenchyma (3) *Hypoplasia*—a miniature kidney which however is normal histologically (4) *Hypertrophy*—an increase in size (5) Change in form—*short, long or round* (6) *Fusion*—the most common is union of the lower poles across the midline to form the *horseshoe kidney* The ureters descend anterior to the renal substance (7) *Ectopia* (dystopia)—presence of the kidney any place between its normal position and the pelvis At or below the pelvic brim is the most common site (8) *Crossed ectopia*—presence of both kidneys on the same side with or without

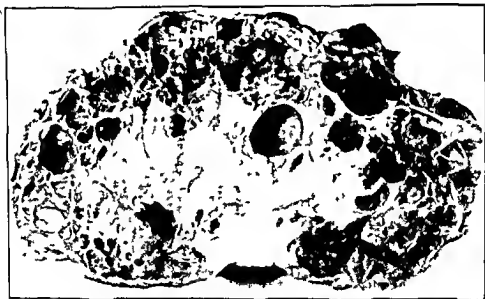


FIG 341—Polycystic kidney

fusion of the two parenchymas (9) *Rotation*—incomplete or excessive (10) *Supernumery kidney*—excess number (usually one) The extra kidney is ordinarily smaller than, and located below, the normal (11) *Cysts* These may be single, multiple or numerous The latter is known as *polycystic kidney* and is congenital Although its *genesis* is still disputed, the present consensus is that the cysts result from faulty fusion of the collecting and convoluted tubules and from persistent primary tubules of the metanephros which ordinarily disappear Most cysts are thus glomerular or secreting tubular Some, however, are excretory tubular, that is, arise from collecting tubules and are said to eventuate from fibrous tissue occlusion of the lumens *Grossly*, the kidneys are normal in size or greatly enlarged, and contain innumerable cysts that are a millimeter or less to several centimeters in diameter (Fig 341) They

are often bluish tinged; contain clear fluid, and are lined with a smooth membrane. Patients with polycystic kidneys die either from renal failure or from hypertension. *Solitary or multiple cysts* are congenital and arise similarly to those in polycystic kidneys, or they are acquired and develop as a result of low grade infection, fibrosis and tubular obstruction. They may measure as much as 15 cm. in diameter. They are clinically significant (1) when they become large enough to be felt and to produce pain, (2) when they cause hypertension and (3) when they become infected.

Inflammations.—Surgically important inflammatory lesions of the kidney consist of (1) non-specific, such as carbuncle, perinephritis and perinephric abscess, and pyelonephritis and (2) specific granulomatous, such as tuberculosis, syphilis and actinomycosis. *Syphilis* of the kidney is rare. It exists as a diffuse parenchymatous or interstitial infection and as a gumma. *Actinomycosis* is also rare and is practically always secondary to lesions of adjacent structures.

Carbuncle of the kidney is similar to carbuncle of the skin, that is, it consists of a collection of pyogenic abscesses in the parenchyma. It is usually *caused* by staphylococcus aureus. The organisms reach the kidney by way of the blood stream from a primary focus in the skin. The cutaneous infection, which is usually a furuncle or a carbuncle, precedes the renal infection from a few days to many months, with an average of about two months. Initially, the *symptoms* are quite vague. There are indefinite pain in the flank, malaise, prostration, fever, chills, tenderness in the region of the kidney and, occasionally, signs of supradiaphragmatic pulmonary infection. The blood culture is occasionally positive and the urine may contain leukocytes and erythrocytes. *Grossly*, the kidney is usually irregularly enlarged and bossed and the capsule is adherent. Cut surfaces disclose one or more acute abscesses. They are sharply circumscribed, irregularly outlined and measure as much as 6 to 8 cm. in diameter. The walls are grey and of varying thickness; the inner surfaces are ragged and necrotic, and the centers are filled with thick creamy yellowish pus. *Histologically*, from within out there are débris, neutrophils and granulation tissue. *Treatment* consists of administration of sulfonamides and antibiotics, such as penicillin. If these are not curative, surgical intervention in the form of incision and drainage, enucleation of the carbuncle or nephrectomy is indicated. The mortality rate in reported cases has been high.

Perinephritis and perinephric abscess are infections of the fatty tissue around the kidney that is within the confines of the renal fascia. The causative *organisms* are many, but the most common ones are staphylococci, streptococci, colon bacilli and tubercle bacilli. The *routes* of infection are (1) hematogenous from foci elsewhere in the body. Usually there are no predisposing local factors, but sometimes there may be preceding renal trauma with a subsequent hematoma, and (2) extension from adjacent organs and tissues. Of these, the kidney heads the list. Other structures are vertebra, lungs, pleura, appendix, colon and pelvic organs. The *clinical* manifestations are similar to those in renal carbuncle. In

addition, there are a mass in the lumbar region and roentgenographic changes. These consist of an enlarged renal shadow, scoliosis of the spine with the concavity directed towards the swelling, deformity of the renal pelvis and obliteration of the psoas shadow.

Grossly, the perirenal space is distended to a flask-like shape with the tapering end directed along the pelvis and ureter. The mass is attached to the diaphragm, psoas muscle, quadratus lumborum muscle, vertebrae, peritoneum and abdominal muscle. The kidney, in the upper portion, is surrounded by densely adherent, grey or hemorrhagic, extremely firm sclerotic tissue or by more edematous tissue that is diffusely permeated with pus or contains frank abscesses. *Histologically*, there are fibrosis, edema and leukocytic and plasma cell infiltration with or without breakdown of tissue.

Treatment consists of administration of sulfonamides and antibiotics (penicillin), supplemented if necessary by surgical incision and drainage. *The death rate in recorded cases has been about 25 per cent.*

Pyelonephritis is an infection of both the pelvis of the kidney and the parenchyma. Formerly much was said about pyelitis—as though the infection were limited to the pelvis. It is now known that such does not occur and that in all cases the renal parenchyma suffers as well. The disease may be acute, chronic or recurrent. Ordinary *pyogenic organisms* may be isolated in the acute or recurrent stages but they cannot be found, as a rule, in the chronic stage. The route of infection is either hematogenous or ascending from the lower urinary tract. The latter is almost always associated with some obstruction to the outflow of urine. If the obstructive lesions are congenital the infection may start in infancy or early childhood, but if they are acquired the age of onset will vary. *Clinically*, the acute infections are characterized by combinations of fever, chills, pain, pallor, tenderness over the kidney, dysuria, pyuria, bacteremia and anemia, while chronic infections may reveal, in addition, hypertension and uremia.

Grossly, the kidney in *acute pyelonephritis* is usually enlarged and swollen. The capsule is adherent, the cut edges are everted, the cortico-medullary demarcations are obscured, there is radial streaking of the parenchyma, and there may or may not be detectable cortical abscesses. The pelvis is dilated and its mucosa is red and covered with an exudate. *Histologically*, the pelvic mucosa may be ulcerated and the tunica propria is edematous, hemorrhagic and infiltrated with neutrophils and lesser numbers of plasma cells and lymphocytes. The interstitial tissue of the renal parenchyma is similarly affected. The capillaries are prominent, engorged and are sometimes filled with thrombi. Scattered throughout, there are collections of neutrophils with breakdown of tissue to form abscesses. The glomeruli and tubules are compressed, distorted and inconspicuous. The lumens of the latter frequently contain neutrophilic casts. In the *chronic and healing or healed stages*, the kidneys are usually reduced in size. If both are affected, the distortion is unequal. The capsules are adherent, often tearing away a portion of the underlying parenchyma. The cortex is finely and, more

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important, deeply and irregularly scarred. Between the latter the renal tissue is hypertrophied. The calyces and pelvis are thick, usually dilated and less often contracted. *Histologically*, the dominant process is fibrous scarring. In these areas, the glomeruli are hyalinized, the tubules are reduced in number, and some are dilated and filled with hyalin casts. In other areas the interstitial tissue is increased in amount and is infiltrated with plasma cells lymphocytes and occasionally macrophages. The smaller arteries and arterioles show intimal fibrosis and concentric increase of connective tissue cells—the so-called proliferative endarteritis.

Treatment of pyelonephritis is directed towards relieving the urinary tract obstruction when it is present, and ridding the patient of the causative organisms by the administration of sulfonamides and antibiotics. If the disease is unilateral and if it is attended by hypertension, nephrectomy is worthy of trial.



FIG. 342.—Caseating tuberculosis of the kidney.

Tuberculosis of the kidney is always secondary to some other focus in the body. It is, of course, caused by the tubercle bacillus which usually reaches the kidney by way of the blood stream. The disease occurs at all ages but is most common between twenty and forty years, and it affects males twice as frequently as females. It is often symptomless until the infection has spread to the pelvis, ureter and bladder. The latter is *attended by* frequency, urgency and dysuria. In more than one half of all cases, there is gross hematuria. There may, in addition, be a dull aching pain or a sense of heaviness in the region of the kidney. Cystoscopy usually discloses the lesions in the bladder already described, and pyelography reveals filling defects. Tubercle bacilli can ordinarily be isolated from a twenty-four hour sample of urine.

The types of renal tuberculosis that are of importance to the surgeon are tuberculoma and the ulcero-caseous variety. *Tuber-*

culoma is rare. Grossly, it exists as a well encapsulated mass of necrotic and caseous tissue that occupies any portion of the parenchyma, that often presses upon and distorts the calyces and pelvis and that usually measures from 4 to 8 cm. in diameter. The *ulcero-caseous* variety is common, and usually starts as a tubercle or conglomeration of tubercles that are located in the medulla. Gradually, these enlarge, coalesce, breakdown and again spread to adjacent tissue until all of the medulla and all but a peripheral rim of the cortex are converted into irregular, communicating abscesses (Fig. 342). When these connect with the pelvis, the necrotic material is discharged with the urine and the lesions remain as cavities. Their inner surfaces are ragged, grey, necrotic and friable and their walls are thick and fibrotic. When the abscesses do not communicate with the pelvis the necrotic and caseous material is retained. A superimposed pyogenic infection often alters the picture. *Histologically*, the characteristic unit is the tubercle and is similar to that in other organs and tissues.

Tuberculosis of the kidney is suspected in the presence of hematuria and symptoms of bladder irritability, particularly in patients with known diseases elsewhere. The *diagnosis* is confirmed by cystoscopy, pyelography and the isolation of tubercle bacilli in the urine. *Treatment* is medical first and only when this fails is it surgical. The latter consists of nephrectomy and is carried out (1) when the renal infection is unilateral and that in other organs is healed or quiescent, (2) occasionally when the renal disease is bilateral, but when one side is extensive and (3) when the pulmonary or other lesions are active, but the renal lesion causes unbearable pain or is retarding healing of the extra-renal disease. Without surgical treatment most of the patients die within three years, whereas over half of those with nephrectomy are alive and well ten years postoperatively.

Tumors—Neoplasms of the kidney have been variously classified. Some of the classifications are simple, while others are complicated. It appears to the author that one based upon histogenesis is just as adequate in the kidney as it is in other organs. Thus from epithelium there arises an adenoma, papilloma and carcinoma, from adrenal rests, a hypernephroma, from primitive embryonic tissue, an embryoma (Wilm's tumor), from blood vessels, a hemangioma and hemangiosarcoma, from fat tissue, a lipoma and liposarcoma, from connective tissue, a fibroma and fibrosarcoma, from muscle, a leiomyoma, leiomyosarcoma, rhabdomyosarcoma and myoblastoma, from lymphoid tissue (reticulum cells), lymphoblastomas including the leukemias, from nerve tissue, a neurofibroma, neurofibrosarcoma and sympathoblastoma, and from distant areas, metastatic tumors. Of the entire group, the three most common and clinically most important tumors are hemangioma, carcinoma and embryoma.

Hemangioma—This tumor is less frequent in the kidneys than it is in the skin and other organs of the body. It is found anywhere in the parenchyma and measures from less than 1 cm. to more than 10 cm. in diameter. It is sharply circumscribed, externally bossed, moderately firm and deep red to purple in color. Cut surfaces are

rather solid and pinkish grey or more frequently, they are sponge-like and filled with blood. *Histologically*, the tumor is of a capillary or cavernous type. It has no predilection for either sex and is most common in the fourth and fifth decades of life. The smaller tumors are usually asymptomatic unless they break into the pelvis when they are accompanied by *hematuria*. Larger tumors may in addition produce inconstant pain and, rarely, they are palpable. *Treatment* is nephrectomy. The *prognosis* is good.

Carcinoma.—This is the most common malignant renal tumor in adults, and it is said to constitute about 2 per cent of all cancers. Its *histogenesis* has been the subject of considerable discussion which has not been resolved even today. It is probable that each



FIG 343 —Carcinoma of the kidney.

of the three main theories accounts for some of the growths. These are (1) that the tumors arise from renal epithelium which is found in the tubules, Bowman's capsule and glomeruli, (2) that they originate from inclusions of totipotent cells of the Wolffian ridge, and (3) that they develop from adrenal nests. The latter theory was proposed by Grawitz who called such lesions *hypernephromas*. Since his contribution, they have also been known as Grawitz tumor and hypernephroid tumor. Carcinoma of the kidney is ordinarily found between the ages of forty and seventy years, and it affects males twice as frequently as females. Sometimes, the lesions are silent and a metastatic focus is the first to attract attention. Sooner or later, however, the majority are *attended by* painless hematuria, pain in the renal area, palpable mass, loss of weight, weakness and anemia.

Grossly, the tumor is usually found in one kidney, but cases of bilateral primary cancers are described. Any portion of the kidney may be affected, although the favored site is at a pole (Fig. 343). The lesion measures from 1 to 30 cm. in diameter. As a rule, it is encapsulated and sharply demarcated from the compressed adjacent renal parenchyma. Its external surface is globular but irregularly bossed. Cut surfaces disclose a flat or slightly bulging variegated mass of tissue traversed by thin or broad fibrous trabeculae. The tumor is orange colored, yellowish, grey or hemorrhagic. It frequently discloses large areas of complete necrosis into which hemor-



FIG. 344

FIG. 345

FIG. 344—Clear cell carcinoma of the kidney $\times 100$

FIG. 345—Papillary carcinoma of the kidney $\times 100$

rhage readily occurs. Foci of calcification may or may not be detected grossly. *Histologically* the most common variety is the so-called *clear cell carcinoma*. This consists of sheets, cords or alveoli composed of large polyhedral often glycogen or fat containing cells (Fig. 344). Their borders are distinct, the cytoplasm stains lightly and is reticulated or vacuolated, and the nuclei are central or slightly eccentric, round, relatively small and evenly stained. Tumor giant cells are sometimes frequent. The cells are often several layers deep and grouped around thin capillaries. At other times, they attempt to form renal tubules. The supporting stroma is usually extremely scanty and is well-vascularized. Necrosis is frequent. The clear cell tumors are often mixed with the *granular cell* variety.

These are composed of much smaller cuboidal or spindle cells that tend to line tubular spaces and collect into tuft-like clusters which resemble glomeruli. The cytoplasm is granular and eosinophilic and the nuclei are small round or oblong and intensely basophilic. A third variety of primary renal carcinoma is the *adenomatous* and *papillary* type. Here the cells are usually cuboidal, quite uniform and regular (Fig. 345). They form acini that resemble renal tubules and they line fibrous or connective tissue stalks to form long or short intra-acinar or intracystic papillae.

Spread of carcinoma of the kidney is by direct extension to the pelvis, renal vein and inferior vena cava and by lymphatics and blood stream to distant areas. The organs most frequently affected are the lungs, bones, liver and lymph nodes. Freak metastases sometimes occur. The author has seen one case in which there was a solitary nodule at the base of the tongue and another case where the parotid gland alone was involved.

The *diagnosis* of renal carcinoma is established from the history, a roentgenogram of the abdomen which may reveal a tumor mass, urograms which show distortion of the calyces and renal pelvis, and, rarely, by finding tumor cells in the urine. *Treatment* is surgical removal followed by irradiation. The five year *survival* rate varies from 15 to 30 per cent.

Embryoma.—This tumor, also known as *mixed tumor* and *Wilm's tumor*, usually occurs in infancy and early childhood, although cases have been recorded in as late as the eighth decade of life. It doubtlessly arises from primitive nephrogenic tissue, affects both sexes with equal frequency, and has no predilection for either kidney. The most common initial *symptom* is swelling of the abdomen due directly to the tumor. Later, there are abdominal pain, loss of weight, constipation, fever, leukocytosis and anemia.

Grossly, the tumor usually measures 10 to 30 cm. in diameter and weighs as much as 3500 gm. It is round, bossed and surrounded by a thin capsule which is often penetrated by tumor tissue. The kidney may be pushed aside, although it is often engulfed or completely destroyed. Cut surfaces disclose light brown or grey soft moist but friable tumor tissue that has the appearance of sarcoma (Fig. 346). There may be scattered foci of necrosis and hemorrhage, but fibrosis or fibrous tissue trabeculae are not prominent. *Histologically*, the cells are round, oval or spindle-shaped (Fig. 347). The cytoplasm is scanty, ill-defined and of a poor quality. The nuclei are round, oval or somewhat distorted, but they are small and hyperchromatic. In some areas, the tissue is solid and dense or myxomatous while in others, it tends to form acini and glomeruli. The supporting connective tissue is so scanty that it is practically non-existent or it is somewhat more abundant and edematous. Thin-walled capillaries while present are not conspicuous. Other elements which are found in these tumors are smooth and striated muscle, bone and cartilage. Embryomas *spread* by direct extension to neighboring organs and tissues, and less often by metastasis to lymph nodes, lungs and brain.

The only life saving *treatment* is surgical extirpation. Although

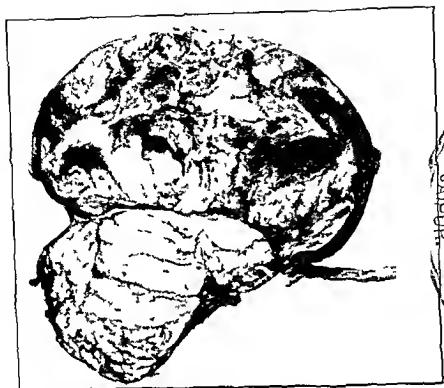


FIG 346—Embryoma of the kidney

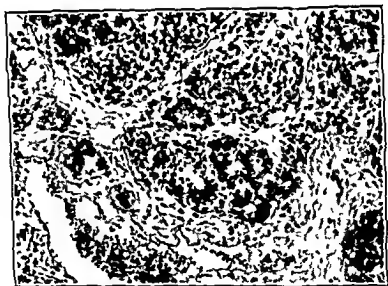


FIG 347—Embryoma of the kidney showing an attempt at acinar formation x 100

these tumors are radio-sensitive, irradiation alone does not prevent recurrences, metastases and death. It may be used preoperatively to shrink the tumor, but some authors contend that one is not justified in delaying operation even that long. The younger the

patient, the better the *prognosis*. Probable cures are reported in as high as 25 per cent of all cases.

Mechanical Disturbances.—These will be briefly considered under the following headings: renal changes in secondary shock, aneurysm of the renal artery, renal hypertension, trauma, bilateral cortical necrosis, nephroptosis, hematuria, urinary calculi and urinary tract obstruction.

Renal Changes in Secondary Shock.—Under this title is included a clinico-pathological entity affecting primarily the kidneys and called hepato-renal syndroma, nephrosis, clinically acute nephritis, acute hematogenous interstitial nephritis, extra renal azotemia, acute interstitial nephritis and crush syndrome. The syndrome has been

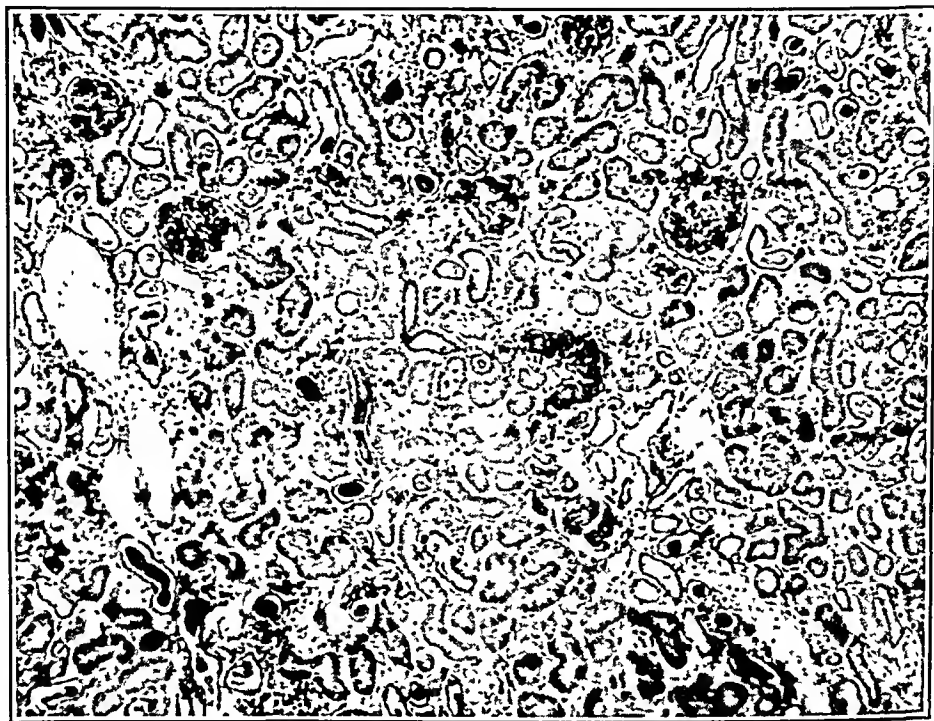


FIG 348—Renal changes in secondary shock illustrating congestion of glomeruli, degeneration of the tubules, casts, and edema and cellular infiltration of the supporting connective tissue. x 60.

described in association with a wide variety of clinical disorders among which are peritonitis, septicemia, abscess, pneumonia, transfusion reactions, postoperative shock, intestinal obstruction, crushing injuries, liver disorders, chemical poisoning by sulfonamides mercury bichloride, carbon tetrachloride, iodides, quinine and cantharidine, and massive destruction of tumor tissue. *Clinically*, the syndrome is characterized by a sudden or insidious onset of peripheral vascular collapse or better known as shock. There are hemoconcentration, drop in blood pressure, increasing oliguria, anuria and either death in uremia or recovery. *Grossly*, the kidneys are enlarged, congested, and show obscuring of the cortico-medullary demarcations, an eversion of the cut edges and swollen cortices. *Histologically*, the glomeruli are normal or congested and contain edema fluid (Fig. 348). The tubules are dilated; their epithelium

is degenerated, necrotic or regenerated, and their lumens contain pigment, hyalin or cellular casts. The interstitial tissue shows edema and an infiltration with plasma cells, lymphocytes and neutrophils. Since the primary conditions are so divergent and since most of them are attended by tissue destruction it is thought that a common cause of the renal changes is a protein or protein split product and that this acts by way of producing peripheral vascular collapse or shock. *Treatment* is primarily medical under which regime many patients recover. In selected cases, renal decapsulation has been performed with good results. Whether these cases would have recovered without operation is impossible to say.

Aneurysm of the Renal Artery—This is not common. While some cases may be of congenital origin, most are acquired and result from anything that weakens the arterial wall. Among such agents are trauma, infection as pneumonia, rheumatic fever, endocarditis, syphilis and periarteritis nodosa, and degenerations as arteriosclerosis. *Pathologically*, renal aneurysms are divided into (1) true—saccular dilatations wherein the wall is weakened, bulges as a whole and contains all the coats, and (2) false—actually an intramural hematoma with destruction of most of the wall. The size varies from a few millimeters to 20 cm. in diameter. The mass may rupture into the pelvis or perirenal tissue and cause hemorrhage, or it may compress the renal artery, produce renal ischemia and result in hypertension. Other manifestations are pain in the loin, palpable mass, rarely hematuria and radiologically an extrarenal tumor which may show areas of calcification. *Treatment*, even in silent cases, should be nephrectomy.

Renal Hypertension—It has been proved beyond doubt, experimentally and clinically, that some cases of hypertension are caused by ischemic renal tissue. Although the exact mechanism is not yet known, it is thought that the juxta-glomerular apparatus secretes a substance called renin which in combination with a pseudoglobulin fraction of the blood (hypertensinogen or renin-activator) releases hypertensin or angiotonin. This causes vaso-constriction and an elevated blood pressure. In man, the causes of renal ischemia may be divided into those that affect primarily the renal artery or its branches and those that affect primarily the parenchyma. The former consist of embolism, thrombosis, arteriosclerosis, periarteritis nodosa, congenital narrowing of lumen, aneurysm of the renal artery, kinks of the renal pelvis, and narrowing of the artery from external pressure by lymphosarcoma, hydatid cyst, aneurysm of the aorta and calcified hematoma. Primary parenchymal lesions causing hypertension are congenital hypoplasia, polycystic disease, pyelonephritis, tuberculosis, rarely renal neoplasms, hydronephrosis, pyonephrosis, nephroptosis and renal trauma. *Grossly*, the ischemic kidney is usually atrophic, while the remaining one is ordinarily normal. *Histologically*, the ischemic kidney shows only a shrinking or degeneration of the parenchyma, while the unprotected kidney may show all the features of malignant nephrosclerosis. The most important of these are arteriolar endarteritis and necrosis. *Treatment* is directed towards removing the cause. If this is unilateral

and if the changes in the unprotected kidney have not progressed to a stage of irreversibility, the chances of cure are good. Otherwise, they are poor for the lesions in the second kidney are then self-perpetuating.

Trauma.—Trauma to the kidney may *result from* penetrating or non-penetrating injury. The former is due to gun shot or stab wounds and rarely affects the kidney alone. The latter is due to kicks, blows or falls that are frequently sustained in automobile accidents, football games and the like. *Clinically*, there is a history of an injury following which symptoms may appear abruptly or may be delayed for hours or even days. If the trauma is severe enough, there is usually primary shock due to injury to the nerve plexus or adrenal gland. Recovery from this is often followed by renal pain, hematuria, exquisite tenderness, abdominal rigidity, palpable renal mass, and profound secondary shock. The actual *damage to the kidney* may consist of (1) local hemorrhagic extravasation with or without subcapsular hematoma, (2) incomplete rupture wherein deep lacerations involve the parenchyma and extend on the one hand through the capsule and on the other through the pelvis, (3) complete rupture wherein the lacerations extend through the capsule, parenchyma and pelvis and (4) tears of the renal vessels at the hilum. There may thus be extensive hemorrhage into the kidney, perirenal tissue and pelvis and, in tears of the pelvis, there are usually urinary extravasation and secondary infection. In most instances, the lesions mend themselves and the patient recovers. In a few, surgical intervention in the form of drainage, nephrectomy or repair is necessary. When the injury is confined to the kidney alone, the outlook is good, but when other organs are affected, the mortality rate is high.

Bilateral Cortical Necrosis.—This is not a surgical problem and is included here only because it enters into a differential diagnosis and because, if the surgeon is not cognizant of the lesion, a nephrectomy may be erroneously performed. The condition is seen in pregnant and non-pregnant patients. In the latter group, males are affected twice as frequently as females, and the most common age period is between the second and fifth decades of life. Scarlet fever, diphtheria, tonsillitis, pneumonia, tuberculosis, and dysentery have been the most common accompanying diseases. *Clinically*, there are extreme tenderness in the loins and epigastrium, albumin, leukocytes, erythrocytes and hyaline and granular casts in the urine, and elevated non-protein nitrogen in the blood. *Grossly*, the kidneys are enlarged; the capsules are not or only slightly adherent; the external surface is of an irregular deep red to almost black mottled appearance; cut surfaces are diffusely affected by variously shaped confluent infarcts that present a mottled light and deep red, pink, grey and yellowish appearance, and the larger veins and arteries are devoid of thrombi or emboli. *Histologically*, the involved tissue is in various stages of degeneration, disintegration and necrosis. The intralobular arteries show necrosis and plugging of their lumens by thrombi. The necrosis doubtlessly eventuates from occlusions of the intralobular arteries but the *cause* of these

occlusions are not known. One explanation is that circulating endogenous or exogenous toxins produce vasospasm which results in paralysis, necrosis of the walls and thrombosis. Since the lesion is bilateral, it is not a surgical problem.

Nephroptosis—This means a dropped or movable kidney that was once normal in position and that receives its blood supply from the usual site in the abdominal aorta. Its causes are listed as an inadequate pocket in the curve of the spine, lack of supporting perirenal fat and absence of the normal capsular "adhesions." It is seen in asthenic persons, in debilitating diseases, after childbirth and after trauma. There are pain around the kidney with radiation to the genitals, nausea and vomiting, and loss of weight. When symptoms are abrupt and severe the condition is referred to as *Dietl's crisis*. Clinical manifestations are due to kinking of the ureter and retention of urine. If the obstruction is unrelieved, there will eventually develop hydronephrosis, infection and calculi. Treatment is conservative in the form of gaining weight, strengthening the abdominal muscles and wearing abdominal supports. If these fail, it consists of nephropexy. For the operation to be successful, one must make certain that other causes of ureteral obstruction are not present.

Hematuria—This signifies grossly visible blood in the urine. It is a symptom and not a disease. Its more important causes may be listed as follows: (1) *Congenital*—polycystic disease of the kidney. (2) *Inflammation*—any portion of the urinary tract chief among which are acute cystitis, tuberculosis of the bladder, chronic prostatitis, pyelonephritis and the various forms of Bright's diseases. (3) *Tumors*—principally papillary neoplasms of the bladder, ureter and pelvis, but also hemangioma of the kidney and pelvis, carcinoma of the kidney and leukemia. (4) *Mechanical*—calculi, varicosities in the bladder and pelvis and trauma. (5) *Systemic*—hemophilia and purpura.

Calculi—Urinary calculi can form, under certain conditions, in any portion of the urinary tract from the renal parenchyma to the external meatus of the urethra. The usual site, however, is the pelvis of the kidney whence they migrate to the lower portions of the tract. The most common constituents of urinary calculi are calcium oxalate, phosphate, urate and carbonate and cystine and uric acid. The sources of these materials are drinking water, food and normal or abnormal break down of body tissues. Ordinarily, the salts are held in the urine in suspension. When, however, they become too concentrated, they precipitate out, and once a nucleus is formed, they adhere to the latter to form the stone. In infected urine the nucleus consists of dead epithelial cells and bacteria, while in non-infected urine it consists merely of cell-like colloidal droplets of the salt which have separated out after they have reached a certain concentration. Initially, these droplets are homogeneous but later, they become crystalline with a radiating pattern. Stones that form within the renal parenchyma are said to arise in the peritubular spaces by ingestion of calcium particles by phagocytes. When these are formed beneath the epithelium of the papilla, they

may be extruded into the renal pelvis and there form the nucleus of a larger stone. The *local causes* of urinary calculi are: (1) *Stasis* of urine. This occurs when there is obstruction to the flow of urine in any portion of the urinary tract and it also occurs in the dependent pelves and calyces of patients immobilized for fractures, osteomyelitis and arthritis. The mechanism here is simply that stagnation allows more time for precipitation and that the precipitate is not washed away. (2) *Infection*. This, and particularly the urea splitting proteus group, renders the urine alkaline and alkalinity helps precipitation of calcium salts. (3) *Hypercalcuria* as seen in hyperparathyroidism and hypervitaminosis D. Sometimes urinary calculi are symptomless, whereas at other times they are *attended by* colicky pain, hematuria, burning on micturition, frequency, chills, tenderness in the flank, and leukocytes and erythrocytes in the urine.

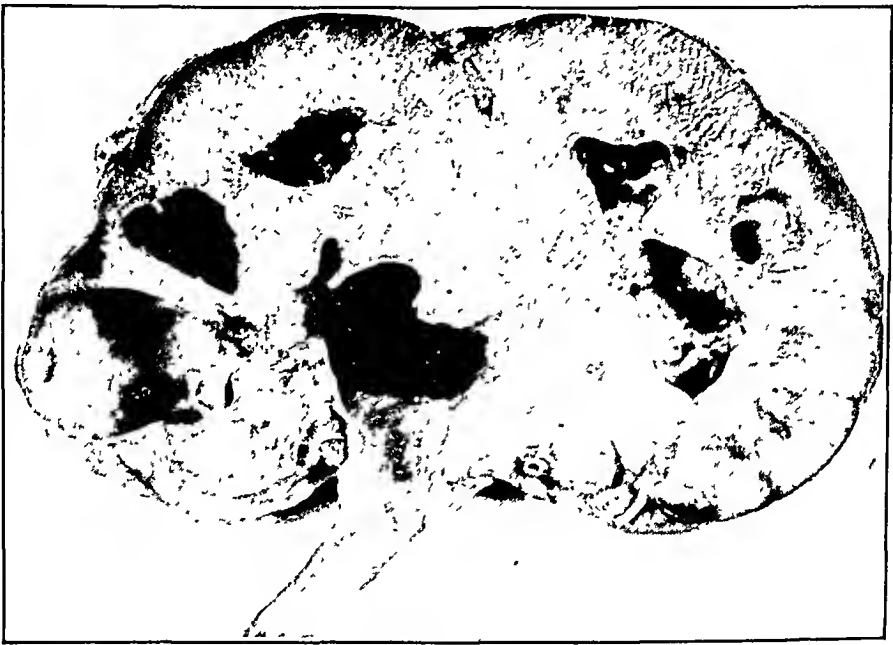


FIG 349 — Calculus in the pelvis of a kidney causing hydronephrosis

Grossly, the stones are variform. When small and in a large cavity such as the renal pelvis and bladder, they are of irregular shapes and sizes. They may be smooth or rough and vary in color from grey to black (Fig. 349). As they increase in size, they are moulded to fit the cavity in which they lie. Such a stone filling the pelvis and calyces of a kidney is referred to as a *stag-horn calculus*. *Treatment* consists (1) of correcting the causative factors, (2) assisting in the passage of the stones when they are being extruded, and (3) of removing them surgically. The ultimate *prognosis* is usually good but the morbidity may be high.

Urinary Tract Obstruction.—This has been considered separately, in the present chapter, under each of the anatomic subdivisions so that only a few general remarks will suffice here. It is obvious that the entire urinary tract is a system of tubes and that when one portion of the tract is occluded, the portion above the obstruction

collects urine and becomes dilated. The causes of obstruction, as has been noted, are numerous. The most common sites are at the urethrovesical, uretero-vesical and uretero-pelvic junctions. If the obstruction is below the entrance of the ureters into the bladder, both right and left ureters and kidneys are affected, whereas if it is above this level, only one side will be involved. The most serious manifestations are reflected in the kidney parenchyma. In the absence of infection and in the presence of gradual obstruction the pelvis and calyces become increasingly distended. The renal tissue is correspondingly thinned, compressed and atrophied so that the normal demarcations gradually become obscured, the entire cortex and medulla are reduced to a mere shell and all function is suppressed. Dilatation of the pelvis of the kidney is known as *hydronephrosis*. If the dilated pelvis becomes infected and filled with pus the condition is then called *pyonephrosis*.

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Chapter XVIII

MALE GENITAL SYSTEM

EMBRYOLOGY

THE early formation of the male and female genital systems are identical. They make their appearance as the urogenital ridges in the 5 to 12 mm. embryo in conjunction with the kidneys. A thickening of the peritoneum on each ventromedian surface produces a bulge, called the *genital ridge*. The superficial cells, known as germinal epithelium, give rise to an internal epithelial mass and to the definitive sex cells. Longitudinal furrows finally separate the gonads from the kidney and intestine after which they become the testes or the ovaries. Originally, both sexes also have male and female ducts. The former consist of salvaged mesonephric ducts and tubules. The latter, known as *Mullerian ducts*, develop from the urogenital ridge on the lateral side of the mesonephros near the cephalic pole. They appear as grooves. The cranial ends remain patent while the caudal ends close to form tubes. These grow inferiorly along the lower ends of the genital ridges, which have meanwhile swung medially to unite in the genital cord. They empty into the urogenital sinus in Muller's tubercle which lies medial to the mesonephric ducts. The two duct systems persist until the sex is well-established, at which time one or the other disappears.

At the 14 mm. stage, the gonads which will become *testes* are recognized by branched anastomosing strands of cells called testis cords and by the appearance between the covering epithelium and the testis cords of the tunica albuginea or capsule. The cords on the one hand give daughter cords which become the seminiferous tubules, and on the other they unite with another series of tubules at the upper pole called rete testis. The early testis cordis are composed of indifferent cells which later give rise to the sex and sustentacular cells of Sertoli. The supporting mesenchyma is differentiated into connective tissue and large interstitial cells. Some of the cranial mesonephric tubules become the efferent ductules of the epididymis and connect with the rete testis while some form the *appendix* of the *epididymis*. The mesonephric duct becomes the *ductus deferens*.

The gonads are originally high in the abdomen. With growth they are gradually left more inferiorly until at ten weeks they lie at the pelvic brim. Later each testis along with vaginal sac of peritoneum descends into the scrotum. In this, it is aided by the gubernaculum testis which is under the influence of the pituitary. The vaginal processes then become separated from the peritoneum and form the *tunica vaginalis*, and the ductus deferens with accompanying nerves, vessels and connective tissue forms the *spermatic cord*. The *prostate* arises as outpouches of the urethra and the *seminal vesicles* form as outpouches of the ductus deferens.

The *external genitals* first appear at six weeks as the genital tubercle. This arises as a midline protrusion from the ventral surface of the body between the umbilicus and tail. At seven weeks, it elongates to form the *phallus* which becomes capped with a rounded tip—the *glans*. At ten weeks, the phallus becomes the *penis*. The edges along the ventral urethral groove grow over and unite to form the *urethra*. Two swellings at the base called labio-scrotal swellings grow caudal, and each produces one half of the *scrotum*. At three months, a fold of skin called the prepuce develops at the base of the *glans* which it covers by five months. At first the adjacent surfaces are fused, but later they again separate except along the under surface of the *glans* where the fusion persists as the *frenulum*. The *corpora cavernosa* develops from the mesenchyma at seven weeks.

PENIS

ANATOMY

The penis in the adult in the flaccid state measures approximately 13 cm in length and 8.5 cm in circumference. It is composed of 3 cylindrical masses, namely, 2 lateral—the *corpora cavernosa penis* and 1 median and posterior—the *corpora cavernosa urethra*. The *corpora cavernosa penis* are attached to the rami of the pubis by *crura*. They are surrounded by a fibrous envelope composed of superficial longitudinal fibers that surround both portions, and deep circular ones that surround each portion and unite medially to form the septum. The *corpora cavernosa urethra* is expanded behind to form the bulb and anteriorly to form the *glans*. It contains the *urethra*. The *penis* as a whole is divided into (1) a *root* which lies in the perineum between the inferior fascia of the urogenital diaphragm and Colle's fascia and is attached to the pubis and suspensory ligament, (2) a *body* forming the bulk of the organ. It is enclosed by a fascia which is connected above to Scarpa's fascia and below to dartos tunic of the scrotum and Colle's fascia and (3) a *glans* which caps the organ. Its tip is pierced by the *urethra*, while its base is expanded to form the corona and back of this the neck. The skin over the penis is loose and dark. At its junction with the *glans* it forms a fold—the *prepuce*. Medially and ventrally the prepuce forms a fold called the *frenulum*. At the neck and corona, there are *preputial glands* which secrete *smegma*. The penis is supplied by the deep and dorsal arteries of the penis which are branches of the internal pudendal arteries. The *venous drainage* accompanies the arteries. The *nerve supply* comes from the second, third and fourth sacral nerves. The *lymphatics* empty into the inguinal nodes.

Histologically, the skin discloses abundant subcutaneous tissue in which there is smooth muscle, but no fat tissue. The fascias are composed of collagen fibers. The *corpora cavernosa penis* and the *corpora cavernosa urethra* consist of a sponge-like system of vascular spaces which are lined with endothelium. They are separated by trabeculae of fibrous, collagenous, elastic and muscle tissue, and are

continuous with both the arteries and veins. The preputial glands are modified subaceous glands.

PATHOLOGY

Congenital Anomalies.—Those concerned with the urethra have already been mentioned (p. 509). Abnormalities associated with the *penis proper* may be listed as follows: absence, concealed (by the skin of the scrotum abdominal wall or perineum), hypoplasia, duplication or diphallus (all degrees from fissuring to complete doubling), torsion, phimosis (stenosis of the orifice of the prepuce), paraphimosis (strangulation of the penis by a stenotic preputial orifice which has been pulled up over the corona), adherence of the foreskin to the glans, absence of the foreskin, short frenulum (which during erection produces ventral curvature of the glans), and epithelial inclusions along the ventral surface.

Inflammations.—The penis, being covered with skin, is subject to any of the cutaneous disorders that have been described in Chapter I and to most of those considered in connection with the anus. The inflammatory lesions may be listed as (1) *non-specific* which includes acute balanitis, furuncles, gangrene, lichen planus, herpes progenerialis, balanitis xerotica obliterans and plastic induration (Peyronie's disease) and (2) *specific granulomatous* which includes tuberculosis, syphilis, chancroid, lymphopathia venereum, granuloma inguinale, and histoplasmosis. *Furuncles* of the penis are similar to furuncles of the skin. *Syphilis* has already been considered in detail in the first chapter. It usually occurs in the primary stage as the chancre, is less frequent in the secondary stage as mucous patches (condyloma latum, and is rare in the tertiary stage as the gumma or diffuse inflammation. *Chancroid*, *lymphopathia venereum*, and *granuloma inguinale* have been described in the section on the anus. *Histoplasmosis* is extremely rare and is similar to that described in the skin.

Acute Balanitis.—This is an inflammation of the glans penis and is usually associated with inflammation of the prepuce. The predisposing *causes* are (1) congenital or acquired phimosis which favors uncleanness, irritation from secretions and collection of smegma, (2) action of chemicals, such as mercury bichloride and phenol, (3) trauma as from tears of adherent prepuce and stones, and (4) metabolic product in the urine, such as sugar, phosphates, creatinine, oxalates and urates. The aforementioned factors favor growth of bacteria which are the exciting causes. The *bacteria* consist of gonococci, Vincent's spirochetes and fusiform bacilli, mixed infections including staphylococci, streptococci and pneumococci and, rarely, diphtheria bacilli. There are itching, burning, pain and discharge. The *prepuce* is inflamed, swollen and indurated. The quantity and quality of the pus varies with the type of infection. The apposing surfaces are congested, dull, covered with pus and superficially or deeply ulcerated. The *histologic* picture is non-specific.

Gangrene.—Gangrene of the penis is not common. It is similar to and often associated with gangrene of the scrotum. While it

may be caused by obstruction to the circulation, direct action of chemicals, severe trauma or injury to "trophic" nerves, it frequently occurs in the presence of minor or insignificant trauma which serves as a portal of entry for virulent streptococci, staphylococci and colon bacilli. Laxity of the subcutaneous tissue allows rapid spread of the infection to involve the entire penis, scrotum, thighs and abdominal wall. The skin becomes red, tense, glossy, hot, tender, painful and edematous. The discharge is usually thin and bloody. A line of demarcation soon appears and within a week the involved portion becomes black and separated as a stringy, foul smelling mass. The condition occurs at all ages, but is most common in the third to fifth decades of life and is usually attended by pain, fever and leukocytosis. Treatment is not standardized but among other things it should include the administration of sulfonamides or antibiotics. The mortality rate is about 20 per cent.

Lichen Planus—This occurs as small flat red papules on the glans penis of adults. *Histologically*, there are hyperkeratosis, acanthosis and hypertrophy or thinning of the rete pegs. In the superficial portion of the corium and dermal papillae, there is a dense infiltration with lymphocytes and few neutrophils. Frequently, the exudate encroaches upon and destroys the basal cells of the epidermis. The lesion is identical with that seen in other areas of the skin.

Herpes Progenitalis—This is characterized by the appearance of small vesicles surrounded by erythema. They occur on the dorsum of the glans or on the prepuce. They may or may not become secondarily infected. Since the lesion disappears spontaneously, it is not seen in the laboratory.

Balanitis Xerotica Obliterans—This inflammation is probably identical with *Baurosis* of the penis. It is a progressive atrophy of the glans that ultimately produces a stenosis of the external meatus. The initial lesions appear as erythematous patches on the prepuce and glans. They are sometimes accompanied by a profuse purulent discharge and ulceration, but more frequently, they are gradually transformed into white atrophic patches and bands. The corona disappears, the frenulum is obliterated, adhesions form between the prepuce and glans, and the prepuce acquires a sclerotic band about 1 cm from its tip. Initially, there is a leukocytic infiltration in the epithelium and papillae. This is later replaced with lymphocytes, epithelioid cells and plasma cells. The inflammatory cells are then resorbed and leave in their stead marked fibrosis. In the late stages, there are atrophy and hyperkeratinization of the epidermis and dense acellular fibrosis of the upper portion of the dermis. The lesion occurs at all ages. Initially, it may be symptomless or it may be accompanied by intense pain, itching, burning and pricking. Later, there is pain on erection, diminution in sensation and interference with sexual function.

Plastic Induration—Plastic induration of the penis is also known as *Peyronie's disease*. It consists of a cord or of plaque-like nodules of induration, located in the midline of the dorsal portion of the penis. The common locations are near the corona or the symphysis

pubis. *Histologically*, the indurations are composed of avascular, acellular fibrous tissue that resembles a keloid. They may contain foci of calcification cartilage and bone. The lesion is usually found in patients beyond the age of forty years. It is accompanied by painful distortion of the penis on erection and increasing difficulty with intercourse. The curvature is usually directed upwards and backwards. *Treatment* has consisted of diathermic or surgical excision or radiotherapy.

Tuberculosis.—Tuberculosis of the penis is rare. It may affect the skin, urethra or cavernous bodies. The *route* of infection is usually direct inoculation and rarely hematogenous. Direct inoculation results from infection of the urinary tract or from disease of the genital organs. In the latter instance, the mechanism is said to be implantation of ejaculated organisms upon the surface of the corona at the time of intercourse. Other methods of contraction have been sucking of the penis during ritual circumcision, buccal coitus and infected clothing. The most common locations of the cutaneous form are the corona and frenulum. The *initial lesion* may appear as a pimple, pustule or ulcer. The latter soon acquires a typical tuberculous appearance. The edges are irregular, sharp and undermined. The floor is first clean and then covered with grey necrotic material and the edges and base are indurated. Adjacent lesions coalesce until the whole corona, glans and, rarely, the entire penis are affected. *Histologically*, the characteristic unit is the tubercle. *Treatment* has consisted of surgical, chemical and electric destruction, and of light and irradiation therapy. It has not been too satisfactory.

Tumors.—Histogenetically, neoplasms of the penis may be classified as follows: from the epithelium, certain “pre-cancerous” lesions, papilloma and carcinoma; from connective tissue, a fibroma and fibrosarcoma; from blood vessels, an angioma and endothelioma; from muscle, a myoma; from fat, a lipoma; from pigment producing cells (melanoblasts), a melanoblastoma; from mesodermal and ectodermal elements, a teratoma, and from distant areas, secondary tumors. Most of the aforementioned neoplasms are extremely rare. “Pre-cancerous” lesions, papilloma, carcinoma and secondary tumors alone merit separate consideration.

“Pre-cancerous” Lesions.—Under this heading the following conditions are often mentioned. (1) *Leukoplakia*. On the penis it is similar grossly and histologically to that seen in the mouth and elsewhere. It exists in the form of glistening white plaques that are located on the margin of the prepuce, the coronal sulcus, the corona, the frenulum and the meatus. *Histologically*, there are hyperkeratosis, hypertrophy of the prickle cell layer, prolongations of the rete pegs and marked lymphocytic infiltration of the papillae and upper portions of the corium. (2) *Erythroplasia of Queyrat*. This consists of one or more well-defined, undermined, indurated ulcers surround by an erythematous area. *Histologically*, there are hyperplasia of the epithelium, hypertrophy of the rete pegs, central denudation of the epithelium and marked erythrocytic engorgement of the adjacent capillaries. (3) *Paget’s disease*. This lesion is

extremely rare Both grossly and histologically, it is similar to Paget's disease of the nipple While it is considered by some authors as precancerous, it is more likely that the lesion is a carcinoma of the sweat glands that has secondarily affected the skin (4) *Bowen's disease* This lesion too is regarded by some as precancerous but by others it is considered as carcinoma in situ It is described in Chapter I

Papilloma—Papilloma of the penis is common There are two chief forms, (1) a peculiar type of wart that discloses excessive and progressive keratosis and is known as the *penile horn* It is prone to cancerous transformation, and (2) conglomerate cauliflower or cock's comb-like masses called *condyloma accuminatum* As already stated in Chapter I, it is not certain whether this lesion is a true tumor or whether it is merely a proliferation of epithelium due to a virus

It is found at all ages but is most common in early adult life Its locations are lining of preputial cavity, the coronal sulcus, corona and less often the glans In most of the cases, the prepuce is long and there is an associated infection At one time the lesions were thought to be of venereal origin and were, therefore, called venereal warts, gonorrheal warts, and venereal vegetations It is now known that the condition has nothing to do with venereal diseases In moist areas, the growths are pink soft friable and easily rubbed off Often they become macerated, ulcerated and impart a most disagreeable odor Histologically, they are composed of papillary proliferations with little keratinization, marked papillary down growth and vascularized connective tissue cores



FIG. 350.—Fungating carcinoma of the glans penis

Treatment has been diversified and includes circumcision, local hygiene, surgical and electric destruction of the growths, irradiation and application of podophyllin ointment

Carcinoma—Carcinoma of the penis is said to comprise from 1 to 3 per cent of all cancers in males The precipitating causes are not known, but the predisposing factors may be listed as follows: chronic inflammation, trauma, old scars, irritation by smegma in the presence of a long prepuce, venereal sores, and the "pre-cancerous" lesions mentioned above Cancer of the penis occurs at any age but is most common in the fifth decade of life and beyond The only symptom may be a mild or severe constant or intermittent itching

In other cases, there are purulent discharge, pain, bleeding, obstruction to outflow of urine, fistulas and "masses" in the groin.

Grossly, the early lesions are variable. They are usually located on the glans or prepuce. They may start as a small wart, a papule, a fissure, an ulcer or a scaly patch. The colors are pink, bright red, dull red or brown. Initially, there is no induration. Sooner or later, however, the lesion enlarges to form (1) a fungating, papillary or cauliflower-like growth (Fig. 350). The surface is grey ulcerated, serrated, and covered with a foul exudate; the pedicle is usually broad, and the base infiltrates the subjacent tissue and is hard; or (2) an infiltrating, penetrating and ulcerating mass. The edges may be elevated or they may be even with the adjoining tissue, but they are always hard and the induration is ill-defined. The floor is covered with grey, necrotic, foul material and the base penetrates the penis to varying depths, often occluding the urethra or perforating it to produce fistulas. *Histologically*, the growth is a squamous cell carcinoma and discloses the usual degrees of differentiation or anaplasia. *Spread* of carcinoma of the penis is, as a rule, by way of the lymphatics to the superficial and deep inguinal nodes which drain into the external iliac nodes and, less frequently, by way of the lymphatics along the dorsal vein which enter the external iliac nodes directly. Visceral metastasis is most common to the liver and is said to occur in 15 per cent of the cases.

The *diagnosis* is often difficult when the lesion is small and usually cannot be made without recourse to a biopsy. *Treatment* consists of (1) irradiation, when the cure rate is reported as high as 62 per cent, and (2) partial or total amputation of the penis with dissection of the inguinal nodes in which case the cure rate is recorded as high as 57 per cent. This lower figure is due to the fact that surgically treated lesions are more advanced. *Death* is usually due to sepsis and cachexia.

Secondary Tumors.—These tumors of the penis are uncommon. They usually reach the organ by metastasis. The recorded primary sites have been prostate, bladder, kidneys, testes, liver, rectum and lung.

Mechanical Disturbances.—These consist of preputial calculi, traumatic avulsion of the skin, incarceration and priapism.

Preputial calculi are found in adults and always in the presence of a long phimotic prepuce. They may be *primary*, when they develop by the deposition of calcium in inspissated smegma or by precipitation of salts from retained urine. *Secondary* stones reach the prepuce by way of the urethral meatus or by erosion through the fossa navicularis. *Symptoms* consist of irritation of the penis, associated with a purulent or sanguineous discharge. The stones can, of course, be readily demonstrated by palpation. *Treatment* consists of slitting the prepuce, removing the calculi, treating the infection and performing a circumcision.

Traumatic avulsion of the skin of the penis and scrotum often results from a trivial injury. The usual story is that the trousers and pubic hair or long prepuce are caught in shafts of motors or gears of farm machinery. The skin is readily torn off with re-

markedly little discomfort to the patient. Treatment consists of chemotherapy or antibiotic therapy together with immediate grafting. It is important to save all pieces of remaining skin for the scrotum has exceptional powers of regeneration.

Incarceration of the penis is due to partial occlusion of the blood supply. The *cause* is some object placed around the organ. The *purpose* in infants and children is to stop enuresis and the objects used are strings and haws. Masturbation and prevention of nocturnal emissions are the motives in adolescent boys and the objects employed are nuts, washers, bottles and rings. In adults, superstition plays the dominant rôle. A wedding ring placed on her husband's penis by the bride on the first night after their marriage is supposed to preserve his potency for life, it is also supposed to cure his gonorrhea, and, in middle aged men, it is reputed to restore waning erectile ability. The *affects* depend upon the object, its tightness and its duration. Thin objects such as string or hair are more cutting than broad bands and are, therefore, often accompanied by urethral fistulas. The usual result is severe edema which may become so extensive that the skin ruptures and the fluid is discharged. The penis becomes greatly enlarged, elongated, tortuous, cold, rubbery, and pale with irregular reddened areas. Gangrene is rarely seen. *Treatment* consists of removing the object and combating the infection.

Priapism is prolonged *erection* of the penis unattended by sexual desire. It may be complete or incomplete, and it may be *due to* central nervous system lesions or disturbances in the cavernous bodies. The latter consists of thrombosis, hemorrhage, inflammatory edema or neoplastic infiltration of the cavernous spaces resulting in obstruction to the circulation. It occurs at all ages, but is most common between twenty and forty years of life, it lasts from a few hours to several years, and it is usually attended by severe pain. *Treatment* consists of inserting a large needle and aspirating the stagnant blood or of incising one of the bodies and expressing the blood clot and blood. Cases of short duration and not due to neoplastic infiltration often recover spontaneously.

PROSTATE

ANATOMY

The prostate measures about 4 x 3 x 2 cm. and weighs approximately 8 gm. It is located between the symphysis and the rectum and surrounds the urethra. Its *base* is directed upwards and is in contact with the urinary bladder. Its *apex* is directed inferiorly and abuts against the fascia of the urogenital diaphragm. The *posterior surface* is separated from the rectum by the prostatic sheath and loose connective tissue. The *ejaculatory ducts* enter the upper border and divide the organ into an upper smaller portion called the median or *middle lobe*, and a larger lower portion which is divided by a shallow furrow into the right and left *lateral lobes*. The lateral lobes are joined in front of the urethra by the *isthmus*. This is

often referred to as the anterior lobe, while the portion of the lateral lobes posterior to the level of the urethra is frequently called the *posterior lobe*. The *anterior surface* lies 2 cm. behind the symphysis pubis from which it is separated by a plexus of veins and fatty tissue. The *lateral surfaces* are covered by the anterior portions of the levator ani muscles. The prostate is enclosed in a sheath which is derived from the pelvic fascia. Its ducts enter the posterior urethra. The *arterial* supply comes from the internal pudendal, inferior vesical and middle hemorrhoidal vessels. The *veins* form a plexus and drain into the hypogastric veins. The *lymphatics* terminate in the hypogastric, sacral and external iliac nodes. The *nerves* come from the pelvic plexus.

Histologically, the prostate consists of 30 to 50 compound tubulo-alveolar glands with 16 to 32 excretory ducts. A basement mem-



FIG. 351.—Normal prostate The acini are regular, lined with cuboidal epithelium, and some contain concretions. x 75.

brane is lacking and the epithelium rests directly upon a layer of dense connective and elastic tissue well-supplied with capillaries (Fig. 351). The lining cells are simple or pseudostratified columnar and often project in thin papillae into the lumens. Their cytoplasm contains numerous lipoid secreting granules. The lumens of the acini often contain concentrically lamellated or homogeneous bodies called prostatic concretions. The supporting stroma is composed of collagenous connective tissue, elastic fibers and smooth muscle.

PATHOLOGY

Congenital Anomalies.—The only developmental malformations of the prostate worthy of note are cysts and diverticula.

Cysts may arise from remnants of Mullerian and Wolffian ducts, or from congenital or acquired occlusions of prostatic ducts. The latter may be due to inflammations or hyperplasia and do not attain

the large size that congenital cysts do. These may measure 6 cm in diameter. They may protrude into the urethra and bladder and, less frequently, laterally or in the midline posteriorly. They are lined with cuboidal or flattened epithelium and their walls are composed of compressed prostatic tissue. Clinically, there may be no symptoms or there may be difficulty in micturition and dysuria. Treatment consists of surgical removal or destruction by transurethral fulguration.

Diverticula of the prostate are either congenital or acquired. *Acquired diverticula* are common. They arise on the basis of previous prostatitis wherein the ducts are occluded and an abscess forms which later ruptures into the urethra. Such diverticula are usually multiple and branched. Their ostia may be large and easily seen with a urethroscope or they may be small in which case the outpocket is demonstrable only in urethrograms. The inner surface is lined by fibrous or granulation tissue and is devoid of an epithelial lining. Rectal examination may reveal nodules that are mistaken for other, and particularly, granulomatous infections. Symptoms and signs consist of pyuria, hematuria, frequency and sexual disturbances. Treatment comprises antibiotic and chemotherapy, prostatic massage and transvesical, perineal or transurethral drainage. *Congenital diverticula* are usually single and are lined by epithelium, unless this has been destroyed by infection. They are asymptomatic and do not, as a rule, require treatment.

Inflammations—Inflammation of the prostate may be divided into non-specific and specific or granulomatous. The latter consist of tuberculosis, syphilis, actinomycosis, that due to coccidioides immitis, and granulomatous prostatitis. Non-specific, tuberculous and granulomatous infections will be considered further.

Non-specific Prostatitis—This is usually caused by direct invasion of organisms from the posterior urethra, although cases of hematogenous infection are sometimes seen. The organisms most frequently encountered are gonococci, staphylococci, streptococci, pneumococci, colon group and diphtheroids. Many of these organisms are normal inhabitants of the posterior urethra, and produce no infection until local resistance is lowered by such conditions as hyperplasia, carcinoma, diabetes, sexual excess and alcoholism. In acute early and mild infections, there may be few or no symptoms, but as the severity increases, and particularly when abscesses are formed, there are urgency, frequency, urethral discharge, pain in rectum, urethra or perineum, fever, leukocytosis and terminal hematuria. By rectal examination, the prostate is enlarged and extremely tender. Cases of *chronic prostatitis* develop from previously acute infections or are insidious from the onset. They disclose frequency, burning on micturition, vague perineal discomfort, terminal hematuria and backache. Histologic examination of *prostatic secretions* in cases of prostatitis discloses single and clumped leukocytes, fibrin, debris and desquamated epithelial cells.

In the hematogenous variety, the organisms lodge in any portion of the gland where they grow and produce destruction of tissue and abscesses. In those arising on the basis of posterior urethritis, the

organisms and the infection reach the gland by way of the tunica propria and interstitial tissue or by way of the lumen of the ducts and acini. In either case the ultimate appearance is similar. *There are* edema, engorgement of capillaries, diffuse infiltration with neutrophils and lesser numbers of plasma cells lymphocytes and monocytes, increase of fibroblasts, permeation of epithelial cells by leukocytes, desquamation of epithelial cells and leukocytes into the lumens, and, in cases of abscess formation, complete breakdown of tissue. As the process becomes more chronic, neutrophils are replaced with plasma cells, lymphocytes and monocytes and there is an ever increasing amount of fibrosis. Some of the acini are occluded and cystically dilated. *Grossly*, the prostate in acute stages is enlarged soft and boggy. When abscesses are formed the organ is often asymmetrical and the affected area becomes fluctuant. When the disease becomes chronic the prostate may be soft and relatively normal, or it may be small, firm and fibrotic. Abscesses of the prostate may be resorbed or they may break into the urethra and less frequently, into the rectum, ischiorectal fossa, buttocks or perineum.

The *diagnosis* of prostatic infection is made from a history of urethral infection followed by frequency, burning and pain on urination, from a rectal examination and from microscopic examination of prostatic fluid. *Treatment* consists of antibiotic and chemotherapy, perineal drainage of acute abscesses, prostatic massage and various types of urethral irrigations.

Tuberculous Prostatitis.—This is practically always secondary to tuberculous infection elsewhere in the body. Most commonly, it is found in some portion of the genito-urinary tract, but sometimes it is present in the lungs, tonsils, lymph nodes and other distant areas. The organ is *grossly* normal, nodular, asymmetrally enlarged or small. It is usually quite firm so that it may be mistaken for carcinoma or prostatic calculi. Cut surfaces disclose no gross abnormalities, grey tubercles, caseating masses or irregular ulcerating cavities. *Histologic* sections are similar to other tuberculous lesions. *Symptoms* are usually those of genito-urinary tuberculosis and only occasionally are they directly referable to the prostate. *Treatment* is directed first to the primary disease. Locally, ultra-violet light, irradiation and radical operation have been performed. The *results* are not satisfactory.

Granulomatous Prostatitis.—This type is important because it may be mistaken for tuberculosis. *Grossly*, the gland shows only benign hyperplasia. *Histologically*, in addition, some acini and ducts are partly or wholly replaced by focal collections of plasma cells, lymphocytes, monocytes and scattered neutrophils. About the periphery there may be a few epithelioid cells and a few giant cells of the foreign body type (Fig. 352). The *cause* is not known, but the lesion is thought to be a foreign body reaction to retained secretions consequent to non-specific prostatitis.

Tumors.—Histogenetically tumors of the prostate may be listed as follows: from the epithelium, benign hypertrophy and carcinoma; from connective tissue, a fibroma, myxoma, fibrosarcoma and

myosarcoma, from muscle, a leiomyoma, leiomyosarcoma and rhabdomyosarcoma, from blood vessels, an angioma and angiosarcoma, from lymphoid tissue (reticulum cells), any of the lymphoblastomas, from nerves, a neurofibroma and neurofibrosarcoma (probably some of the spindle cell sarcomas that have been described), from mesodermal elements as a result of metaplasia (reticulum cells), a chondroma and chondrosarcoma, and from distant areas, metastatic tumors. Benign hypertrophy, carcinoma and sarcomas in general will be considered further.

Benign Hypertrophy—Benign hypertrophy of the prostate is also known as benign hyperplasia, benign prostatic enlargement, benign enlargement, adenoma, adenomatous hyperplasia, nodular hyperplasia and fibro-glandular hyperplasia. It is the most common



FIG. 302.—Granulomatous prostatitis showing a periacinar nodule of epithelioid cells, lymphocytes, a collection of neutrophils and a spurious foreign body giant cell. $\times 100$

tumor in males, being present in over 75 per cent of all men by the time they have reached the ninth decade of life. It is distinctly rare before the age of forty years and has not been recorded before the age of twenty years. Its cause is unknown although the assumption is that it has something to do with a hormonal "unbalance." At one time it was thought that the hypertrophy occurred in the remnants of the Mullerian ducts which correspond to the female uterus, and the cause was considered as a decrease in male sex hormone. It is now known that the enlargement starts in most cases in the lateral and less often in the median lobes of the prostate. This attractive explanation, therefore, does not necessarily hold. The clinical manifestations are, frequency of micturition, nocturia, urgency, difficulty in starting the stream, slow stream, prolongation of micturition, terminal dribbling, urinary retention, pseudopriapism with sexual excess, intermittent hema-

turia, occasionally severe hemorrhage, and by rectal examination a firm elastic enlargement of the prostate.

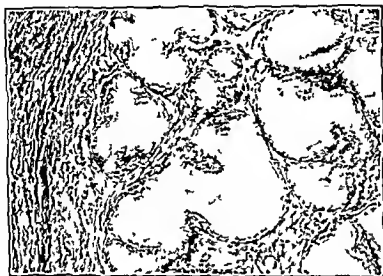
Grossly, enlargement may start wherever there are prostatic glands or ducts but usually it is near the urethra (Fig. 353). As growth proceeds, the nodules become larger and more sharply separated from the compressed adjacent parenchyma. They are composed of whorls of greyish white, moderately firm, somewhat elastic tissue, that frequently bulge above the cut surface. Occasionally they may contain ill-defined yellowish or even greenish areas, and they are almost always associated with an excess amount of milky fluid that drips freely from the cut surface. In advanced cases, the entire prostate becomes enlarged both anteroposteriorly



FIG 353 —Benign hypertrophy of the prostate involving principally the median lobe
The bladder wall is thickened and trabeculated.

and transversely and may weigh as much as 800 gm. The original prostate becomes compressed peripherally to form a mere shell—the pseudocapsule which blends with the true capsule. The external surface is, however, usually smooth. The urethra is almost always elongated and distorted. The appearance of the vesical portion of the prostate varies. Although both the median and lateral areas are usually affected, the enlargement is rarely symmetrical. Sometimes, there is only a ball-like enlargement of the median lobe; at other times, this portion forms a bar across the urethra; at other times still, one or both lateral lobe enlargements dominate the picture so that on cross section the urethra is reduced to a Y or X shape. *Histologically*, all three of the main constituents of the prostate, namely, glandular, muscle and fibrous tissue participate

the hypertrophy. Moreover their participation is uneven so that in some cases the fibromuscular elements overshadow the nodular increase and in others the reverse is true. The fibrous muscle tissue except for being increased in amount does not differ from that of normal prostates. Sometimes, it surrounds the ducts and glands while, at other times, it grows into their lumens and gives a picture that is analogous to peri-canalicular and intra-canalicular fibro-adenoma of the breast. The glands are large, increased in number, show papillary infolding and are lined with columnar, low columnar or cuboidal epithelium (Fig. 354). The cytoplasm is homogeneous, granular or vacuolated and the nuclei are round or oval, vesicular and basilar. Prostatic concretions



354 — Benign hypertrophy of the prostate showing numerous glands with papillary infoldings that are lined with creeling columnar epithelium. $\times 70$

are not present and the surrounding tissue often contains leukocytes.

The diagnosis of hypertrophy of the prostate is made from the history and rectal examination. It may, however, be impossible to distinguish it from infections, carcinoma or calculi. The greatest complication of prostatic enlargement is urinary obstruction and nephritis. Treatment consists of transurethral resection or enucleation of the mass. The prognosis is good.

Carcinoma — Carcinoma of the prostate is one of the commonest malignant tumors in men. It accounts for over 8000 deaths annually in the United States. Its cause, as in other carcinomas, is not known. It can be found in any patient beyond twenty years of age, although it is most common after the fifth decade. The incidence has been reported as varying from 14 to 46 per cent of all men beyond the age of fifty years. Early, there are no symptoms; as the disease progresses there are frequency, difficulty in urination, nocturia, urinary retention, hematuria, incontinence, loss of weight,

anemia, cachexia, and pain in the bones. Rectal examination in early cases may be normal. Later, it discloses asymmetry of the prostate, a hard nodule or, in more advanced cases, a diffuse stony hard mass. The serum acid phosphatase is elevated in about 50 per cent of cases with bone metastasis. In roentgenograms, the latter usually disclose an osteoblastic process.

Although any portion of the prostate can serve as the starting point of a carcinoma, the most common site is the posterior lobe. *Grossly*, the earliest lesions are not detectable and, since they are picked up histologically only, they are often called *occult carcinomas*. As the growth enlarges, it produces ill-defined, greyish white or yellowish grey, firm rather dry and scirrhous nodules that occupy varying proportions of the gland (Fig. 355). Less frequently, the



FIG 355 —Early carcinoma of the prostate The ill-defined nodules as indicated by the arrows are found only in the posterior portion of the gland.

tumor is bulky, soft, grey and encephaloid. In either case the growth ultimately infiltrates the entire gland, projects into the urethra and bladder, obstructs the ureters and extends into the seminal vesicles. *Histologically*, carcinoma of the prostate is extremely pleomorphic. At one extreme there is a well-differentiated growth that deviates but little from the normal. The acini are of moderate sizes or small and the lining cells maintain their polarity. They are columnar or cuboidal and have definite borders, dense acidophilic cytoplasm, deeply stained round or oval nuclei, and no papillae. The chief distinguishing feature is the infiltration of the stroma as evidenced by the absence of the normal condensation of the periacinar collagenous tissue. Another unmistakable criterion of the cancerous nature is the presence of epithelial cells or acini in the peri-neural lymphatic channels (Fig. 356). From this well-differentiated type, there are all gradations from instances where

the cells become taller, their borders less distinct, their polarity lost, the acini less regular, the cytoplasm reticulated or vacuolated and the nuclei more bizarre to instances where the cells are completely anaplastic. Here the cells permeate the stroma in sheets or singly. They are round, oval, spindle or bizarre. Their cytoplasm is scanty or moderate in amount and eosinophilic and the nuclei are small, round, oval or irregular and intensely hyperchromatic (Fig 357). In all cases the stroma may be abundant, dense, acellular, vascular and permeated with leukocytic cells or

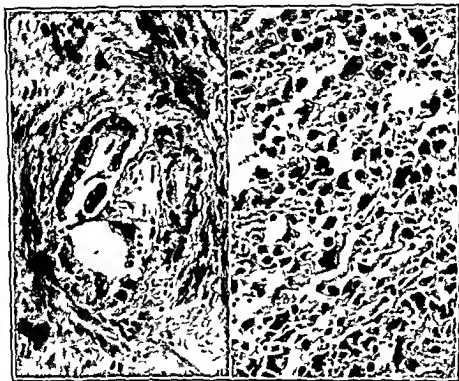


FIG 356

FIG 357

FIG 356 — Well differentiated adenocarcinoma showing invasion of the perineural lymphatics $\times 100$

FIG 357 — Anaplastic carcinoma of the prostate. The cells are extremely irregular and disclose hyperchromatic bizarre nuclei $\times 100$

it may be scanty. Carcinoma of the prostate spreads by continuity, by perineural and other lymphatics and by the blood stream. Metastasis occurs to the lymph nodes, liver, lungs, adrenals, other tissues and bones. In order of frequency, the latter consist of pelvis, sternum, lumbar spine, femurs, dorsal spine, ribs, shoulder girdle, humeri, cervical spine and skull.

The diagnosis of carcinoma of the prostate is established from the history, rectal examination, elevated serum acid phosphatase, roentgen changes in the bones and the demonstration of neoplastic cells in prostatic secretions. It is confirmed by histologic examination of tissue obtained by transurethral resection, by perineal

exposure or by suprapubic enucleation. *Treatment* is radical prostatectomy. If the lesion is too extensive for this procedure, orchidectomy or some form of estrogenic therapy is indicated. The *cure* rate is extremely low. Under the best conditions radical prostatectomy has eradicated the disease in less than 50 per cent of patients operated upon. Hormonal therapy, while palliative only, has prolonged life considerably and has at the same time rid the patients of prostatic obstruction, pains in the bones and cachexia.

Sarcomas.—Sarcomas of the prostate are rare. Although they differ histologically according to the tissue from which they arise, they have a great deal in common. Their onset is insidious and they grow to as much as 15 to 20 cm. in diameter. They *penetrate* in all directions, namely around the urethra, into the bladder, anterior to the bladder along the abdominal wall, posteriorly to the rectum, inferiorly to the perineum, and fill the pelvis where they infiltrate the nerves and erode the bones. *Symptoms* and signs are, therefore, quite varied. Sarcomas of the prostate usually occur in infants and boys, and are rare after the age of fifty years. *Treatment* of choice is radical excision, but the tumor is usually so well-established when discovered that such a procedure cannot be undertaken. Irradiation is, therefore, almost always employed. The *prognosis* is poor.

Mechanical Disturbances.—Two lesions that may be placed in this category are infarct and calculi.

Infarcts of the prostate, as elsewhere, are *caused by* an interruption in the blood supply. This may occur as a result of arteriosclerosis, embolism, stasis because of long recumbency, hypertension, infection and trauma from catheters, sounds, cystoscope, resectoscope and digital rectal examination. The lesion is a common finding in benign hypertrophy. *Initially*, it exists as a circumscribed, sharply demarcated hemorrhagic area that protrudes above the cut surface and that measures 0.5 to 1 cm. in diameter. Later, the area becomes grey, yellowish and softer and is ultimately replaced with fibrous tissue. It may become infected. *Histologically*, the normal architecture is at first still maintained although the cells stain poorly. Later, they degenerate completely. Erythrocytic extravasation is marked and about the periphery the normal acini undergo a metaplasia to a stratified squamous cell type. These cells fill the acini and may be mistaken for an early carcinoma. *Clinically*, infarcts are often asymptomatic, but they may produce pain and urinary difficulty. The lesions are usually removed along with the hypertrophied gland.

Calculi in the prostate are common. There may be *endogenous* or *exogeneous*. The former eventuate from a deposition of calcium phosphate and calcium carbonate about corpora amylacea in stagnant secretion. The latter result from deposition of these salts around calculi that have originated in the upper urinary tract and that have been arrested in the posterior urethra. As a result of pressure they burrow into the prostate. Endogenous

stones are often associated with benign hypertrophy and, therefore, have no distinctive *manifestations*. Exogenous stones may be associated with cohe, hematuria and vesical neck obstruction. The *diagnosis* is made by rectal examination and roentgenography. *Treatment* is removal by prostaticomy or by prostatectomy.

SEMINAL VESICLES

ANATOMY

The seminal vesicles are two outpocketings, one from each ductus deferens, that measure about 5 cm in length. Each consists of a coiled branched tube that is directed upwards and laterally from its opening in the ejaculatory duct. The anterior surface is in contact with the base of the bladder while the posterior surface is separated from the rectum by the recto-vesical fascia. The arteries come from the middle and inferior vesical and middle hemorrhoidal arteries, the lymphatics drain into the hypogastric and external iliac nodes, and the nerves are derived from the pelvic plexus. *Histologically*, there is (1) a mucosa of pseudostratified columnar epithelium, (2) a thin submucosa, (3) a layer of smooth muscle and (4) an external connective tissue sheath.

PATHOLOGY

Congenital Anomalies—Developmental malformations consist among others of absence, hypoplasia, duplication, stricture of the ejaculatory duct and entrance of an ectopic ureter.

Inflammations—Seminal vesiculitis shares in most infections of the posterior urethra and the prostate. The most common afflictions are gonococcal, acute non-specific and tuberculous. There also has been described an acute congestion with retention of secretions and symptoms simulating acute appendicitis. This appears to follow prolonged continence after a period of active sexual life. Massage of the vesicles with release of thick gelatinous secretions is followed by disappearance of symptoms.

Tumors—While neoplasms in the region of the seminal vesicles are not uncommon it is extremely difficult to be certain whether they are primary or secondary in these organs. Bearing this in mind the following may be listed: from epithelium, hyperplasia, cystadenoma and carcinoma, from connective tissue, a fibroma and fibrosarcoma, from muscle, a myoma, from embryonal structures, embryomata, and from adjacent organs and tissues, secondary tumors.

Mechanical Disturbances—These consist of (1) calcification which follows inflammation or senile atrophic changes in the muscle, (2) calculi. True calculi are extremely rare but calcific sequestra from a tuberculous infection are not unusual and (3) trauma from operations upon the rectum, bladder and prostate.

EPIDIDYMIS

ANATOMY

The epididymis is a flattened body composed of a tortuous canal that is attached to the lateral portion of the posterior border of the testis. It consists of (1) a *head* or *globus major* which is closely connected with the testis through the efferent ductules of the gland, (2) a *body* or central portion covered by a reflection of the tunica vaginalis and separated from the testis by connective tissue and (3) a *tail* or *globus minor* also separated by connective tissue and covered by tunica vaginalis. From the tail emerges the *ductus deferens*. Five *sessile bodies* are found in the vicinity of the epididymis. (1) *Appendix* of the *testis* or *hydatus* of Morgagni located on the upper part of the testes just beneath the head of the epididymis. It represents the upper end of the Mullerian duct. (2) *Appendix* of the *epididymis* attached to the head and representing a remnant of the mesonephros. (3) Two *vas aberrans*, one attached to the efferent ductules opposite the appendix of the testis and the other to the side of the tail at its junction with the vas deferens. (4) *Paradidymis* attached to the vas at the level of the head. The blood supply, lymphatics and nerves are the same as those of the testicle. *Histologically*, the proximal portion of the epididymis is lined by tall pseudostratified columnar epithelium whereas the distal portion is lined by lower epithelium. The mucosa rests upon a basement membrane which is surrounded by numerous capillaries and a circular layer of smooth muscle.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the epididymis are not numerous or common. They may be listed as follows. (1) *Cysts*. These consist of enlargement of the appendices normally found, of those developing from retention of secretion and of those that form part of a tumor. (2) *Failure of union* of the epididymis with the testis so that the testis may be found in the inguinal canal and the epididymis in the scrotum. (3) The presence of *ectopic adrenal tissue*.

Inflammations.—Inflammations of the epididymis may be enumerated as follows: (1) *Acute non-specific*. The most common is that due to gonococci which is said to occur in from 5 to 20 per cent of all cases of gonorrhea. Since the advent of antibiotic and chemotherapy, however, these figures are considerably lower. Aside from gonorrhea, any infection of the posterior urethra, prostate or seminal vesicles may ascend to the epididymis. The most common organisms are staphylococci, streptococci and colon bacilli. (2) *Specific or granulomatous*. These consist of syphilis, blastomycosis, filariasis and tuberculosis. The latter is by far the most common. The disease is always secondary to tuberculosis elsewhere in the body, and, while hematogenous infection does occur, direct extension

by way of the ductus deferens from lesions in the prostate, seminal vesicles or urinary tract is the chief route of contraction. The disease may be unilateral or bilateral, develops acutely or insidiously, and, although it occurs at all ages, it is most common between sixteen to forty years. The testis becomes affected secondarily and scrotal fistulas develop in over one-third of all cases. Grossly and histologically, the lesions are similar to those of other organs. *Treatment* consists of antituberculosis measures and epididymectomy. The prognosis, because of associated tuberculosis, is poor.

Tumors—Neoplasms of the spermatic cord, epididymis and testicular tunics are infrequent enough to warrant only a listing. In the *spermatic cord* there have been described from epithelial cells, a cystadenoma and carcinoma, from connective tissue, a fibroma, myxoma, fibrosarcoma and myosarcoma, from vessels, a lymphangioma and hemangioma, from muscle, a leiomyoma, leiomyosarcoma and rhabdomyosarcoma, from fat, a lipoma and liposarcoma, from embryonal structures, a dermoid cyst and teratoma, from reticulum cells, most of the lymphoblastoma, from mesodermal elements (reticulum cells) as a result of metaplasia, an osteoma, chondroma, osteosarcoma and chondrosarcoma, and from distant areas, secondary tumors. In the *epididymis*, the neoplasms that have been described are from epithelium, an adenoma and carcinoma, from mesothelium, a mesothelioma, from connective tissue, a fibroma and fibrosarcoma, from mesodermal tissues, a sarcoma, from embryonal tissues, a teratoma, from fat, a lipoma, from vessels, a hemangioma, lymphangioma and "lymphoendothelioma," and from muscle, a myoma. In the *testicular tunics*, there have occurred from mesothelium, a mesothelioma, from fat, a lipoma, from muscle, a myoma, from lymphatics, a lymphoendothelioma, from connective tissue, a fibroma, and from mesodermal tissues, tumors that have been called simply sarcoma.

Mechanical Disturbances—Two conditions of the epididymis that fall in this category are (1) *infarction* which results from torsion of the spermatic cord and (2) *spermatocele*. These are dilatations of the seminiferous tubules, the epididymis, the vas aberrans, the efferent ducts of the testicle or the paradidymis and usually follow trauma. They are thin walled cysts with a capacity of as much as a quart. The fluid is thin, milky and contains spermatozoa. The wall is lined by columnar or flattened epithelium. Under this heading may also be included a dilation, tortuosity and varicosity of the veins of the spermatic cord known as *varicocele*. This arises either spontaneously or rarely as a result of occlusion of the spermatic vein by tumor. The lesion may be associated with pain, and it presents itself as a mass of soft cord-like structures that is situated above the testicle and in front of the vas deferens.

TESTICLE

ANATOMY

The testes are oval structures that are suspended in the scrotum by the spermatic cords. Each measures about 5 x 3 x 2.5 cm. and weighs approximately 12 gm. Except for a small portion of the posterior border, the testicle is covered on all sides by the visceral layer of *tunica vaginalis*. Immediately beneath this, there is a dense fibrous investment that is called the *tunica albuginea*. The lateral and posterior border of the testicle is covered by the epididymis and all but the posterior border is surrounded by the cavity of the tunica vaginalis. The latter represents the unobliterated lower portion of the vaginal sac of the peritoneum and is surrounded by a visceral layer covering the testis and a parietal layer lining the scrotum. The *arterial* supply comes from the testicular artery which arises from the aorta. The *veins* unite to form the pampiniform plexus which is distributed about the spermatic cord and ends in a spermatic vein. The left one empties into the left renal vein and the right one into the inferior vena cava. The *lymphatics* drain into the pre-aortic lymph nodes. The *nerves* arise in the renal and aortic plexus and from the tenth thoracic nerve.

Histologically, the tunica albuginea consists of dense fibrous tissue and from its posterior surface or mediastinum, sends septa into the gland. Its inner surface contains many blood vessels which form the tunica vasculosa. The latter layer continues into the gland to form the interstitial stroma between the seminiferous tubules. It is composed of collagenous fibers, blood vessels, lymphatics, nerves, fibroblasts, macrophages and interstitial *cells of Leydig*. These cells are located in the angular spaces between the tubules. They are polyhedral with processes or are smaller round or elongated. The nucleus is spherical or irregular, contains coarse chromatin and one or two nucleoli, and is surrounded by a clear zone. The cytoplasm contains neutral fat, lipoids and lipofuscin. The *seminiferous tubules* are surrounded by a basement membrane. Upon this, rest the sustentacular *cells of Sertoli* which are separated by spermatogenic cells. The outlines of the former are indistinct or polygonal; the cytoplasm is reticular, and the nuclei are vesicular, wrinkled, oval and contain one nucleolus. Also along the periphery are *spermatogonia*—round, oval or polygonal cells with granular cytoplasm and round nuclei that contain finely powdered chromatin. By division and maturation these cells ultimately form spermatozoa.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the testicle are numerous. There may be: (1) *Failure of descent* wherein the organ may be intra-abdominal, at the abdominal ring or in t

inguinal canal (the latter being frequently accompanied by hernia) If one testicle is involved the condition is known as *monorchism* whereas if both sides are affected it is called *anorchism*. The latter is often associated with hypogonadism and in both the incidence of malignant tumor formation is greater than in descended testicles. (2) *Aplasia* or *hypoplasia* unilateral or bilateral. (3) *Supernumerary testicle*, usually one sided and just above the epididymis. (4) *Splenic or adrenal inclusions*. (5) *Hermaphroditism*—a person possessing active testicular and ovarian tissue. Usually these are together in one organ which is called an ovotestis, but at other times one organ is a testis and the other an ovary. The proportion of male to female varies, but both are pronounced enough to prevent the victim from being classed as one or the other. A *pseudoher-*

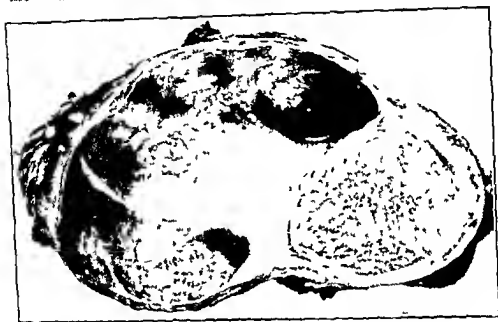


FIG. 358.—Uninfected hydrocele illustrating a thin sac with a smooth mucous lining.

maphrodite is a person having only ovaries or testes with a female or male body development respectively, but with malformations of the external genitals of sufficient degree to resemble the opposite sex. (6) *Hydrocele*. This is an accumulation of serous fluid within the cavity of the tunica vaginalis. It results from trauma or infection or its cause is unknown. Occasionally, it is found in newborn infants but, more frequently, the condition is acquired and found at any time thereafter. The amount of fluid varies from a few cubic centimeters to 5 gallons, and the collection is usually within the scrotum but it may also extend into the abdominal cavity. Unless infected the sac is thin, pale, smooth and white (Fig. 358). When infected it becomes thick, grey and fibrous. The epididymis is, as a rule, acutely or chronically inflamed and enlarged or atrophic. Congenital hydroceles may disappear spontaneously. Acquired ones are treated by aspiration and injection of sclerosing fluid.

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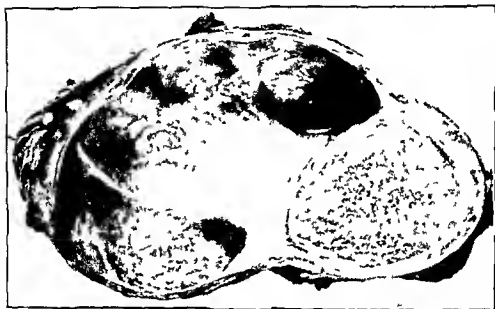


FIG. 358.—Uninfected hydrocele illustrating a thin sac with a smooth inner lining

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PATHOLOGY

Congenital Anomalies.—Developmental malformations of the testicle are numerous. There may be: (1) *Failure of descent* wherein the organ may be intra-abdominal, at the abdominal ring or in the

by originally similar cells that have undergone sexual reversal. The cause of these tumors is not known, but trauma is quoted as a frequent accompaniment and the growths are more common in undescended testicles than they are in those that have reached the scrotum. They are reported as constituting about 1 per cent of all malignant tumors of males and about 4 per cent of all malignant tumors of the genitourinary system. They occur at all ages but are most common in the third and fourth decades. *Symptoms* and *signs* consist of a painless swelling of the testicle in 85 per cent of the cases, pain in 6 per cent of the cases, heaviness in the scrotum, loss of weight, anorexia, cough, backache, gynecomastia, and a firm, rubbery swelling of the testicle. It is said that quantitative gonadotropin assays on the urine exceed the upper limit of normal (20 rat units) in practically all of the malignant tumors of the testicle.

Grossly, the growths vary greatly in size from those detectable microscopically to those measuring, as a rule, less than 10 cm in diameter (Fig 359). A part of the testicle may be affected or the



FIG 359 — Malignant tumor of the testicle (seminoma) replacing almost all of the normal organ. Natural size.

entire organ may be replaced with tumor and the normal shape may be retained. The tunica albuginea is, as a rule, intact, glistening and greyish white. The consistency is firm. In some cases, the cut surfaces are solid pinkish grey, brown and homogeneous or necrotic and hemorrhagic. In others, there are frank cysts filled with clear turbid or greasy material and rarely containing hair. There may be grossly detectable cartilage, foci of calcification or bone. Spread is by lymphatics to periaortic, iliac, diaphragmatic and mediastinal lymph nodes and by blood stream to the lungs. *Histologically*, numerous classifications have been proposed. For practical purposes they may be divided into the following four categories, bearing in mind of course that combinations and transi-

by operation with excision of a portion of the tunica vaginalis and eversion of the rest around the testicle.

Inflammations.—Inflammatory lesions of the testis are essentially the same as those of the epididymis. They consist of: (1) *Acute non-specific orchitis*. This occurs following trauma to the organ, as part of a generalized infection, as extension from acute epididymitis and in association with *mumps*. The latter is usually unilateral and is found about eight days after the onset of the parotid infection but it may precede parotitis. Symptoms may be few and mild or they may consist of chills, fever, testicular pain, nausea and vomiting. The testis is enlarged and edematous and the tunica vaginales contains an excess of fluid. Histologically, there is some leukocytic infiltration but the emphasis is placed upon hyaline degeneration of the tubules. If the disease is bilateral, it usually results in sterility. (2) *Actinomycosis*. This is rare as a primary disease of the testicle but is somewhat more common as an extension from the scrotum. (3) *Filariasis*. Genital infestation with filaria occurs in about 72 per cent of cases, and it affects the spermatic cord, epididymis or the testicle. Early in the disease, the scrotum is red and its contents are swollen painful and tender. As the process becomes chronic, the organs become fibrotic and the edema becomes increasingly severe and permanent. The histologic changes are similar to those already described in Chapter XVI (p. 488). (4) *Tuberculosis*. This is practically always secondary to tuberculosis of the epididymis. When the lesion is recognizable grossly, there are present small pin point tubercles or more frequently areas of caseation, liquefaction, cavitation and fibrosis. Histologically, it resembles other tuberculous processes. (5) *Syphilis*. Unlike in tuberculosis syphilitic lesions of the testis are practically always primary and when the epididymis is involved it is by extension from the orchis. The testis may be enlarged or atrophic. It is usually firm, rubbery and upon pressure is devoid of the usual sensation. Histologically, the process is diffusely granulomatous and with healing becomes replaced with fibrotic scar tissue or it is typically gummatous.

Tumors.—Neoplasms of the testis proper are unique for while some of the histologic components are occasionally represented (such as hemangioma, fibroma, lipoma, neurofibrosarcoma, melanoblastoma and lymphosarcoma) the great majority are derived from germinal epithelium and a few from the interstitial cells of Leydig. For want of a better all inclusive term, the former are referred to as malignant tumors of the testicle. Metastatic neoplasms of the testis are sometimes encountered but they are only of academic interest.

Malignant Tumors.—These tumors of the testicle are probably all teratoid in nature, although frequently there is a one sided development of one of the component elements. The exact point of *origin*, however, has not been agreed upon. It is said that they arise (1) from fetal remnants or inclusions, (2) from undifferentiated cells of the seminiferous tubules—the spermatogonia and (3) from spermatogonia or their derivatives which have been autofertilized

This tumor in the testicle is similar to a similar growth in the uterine cavity. It is attended by massive necrosis and hemorrhage and consists of disorderly arranged masses of both Langhans' and syncytial cells. Large bizarre multinucleated giant cells are sometimes quite numerous.

The clinical *diagnosis* of malignant tumor is often difficult and frequently impossible. It must be differentiated from all other swellings of the testicle, tunica vaginalis and epididymis. Hormonal assays will often be of value, but, at other times, the correct diagnosis is arrived at by a process of exclusion. *Treatment* consists of orchiectomy followed by irradiation therapy. The *prognosis* is guarded. The outlook is best in the adult teratoma and poorest in chorioepithelioma. The five year survival rate is listed as varying from 6 to 58.8 per cent.

Interstitial Cell Tumors (of Leydig)—These tumors are rare. They have been described at all ages. Some are attended by an excess production of androgens but others are not. Gynecomastia is the only *symptom* after puberty, but in children there is precocity. The tumors may be malignant or benign. They are usually less than 2 cm. in diameter, well encapsulated, solid and yellow or yellowish brown in color. *Histologically*, they resemble atrophic adrenal tissue or liver tissue. They are arranged in cords that are separated by acellular well-vascularized fibrous tissue. The cell borders are sharp or indistinct, the cytoplasm is relatively abundant and is filled with fine pink granules, and the nuclei are round or oval, hyperchromatic and contain one or more eccentric nucleoli.

Mechanical Disturbances—Under this heading may be included the following: (1) *Trauma*. This results from a direct blow or crushing injury and brings about petechial hemorrhages, massive hemorrhage or rupture of the tunica albuginea. The condition is important from the standpoint of compensation because it may be followed by infection or be associated with a malignant tumor. (2) *Torsion* of either the appendix of the testis or of the spermatic cord. Each is accompanied by occlusion of the blood supply and, if this is severe enough, by gangrene. If the twist of the cord is outside of the tunica vaginalis, the tunica itself, the epididymis and the testis are all affected. If it is within the tunica vaginalis, only the testes and epididymis will be involved. Most of the patients are between the ages of ten and forty years, the right side is involved as frequently as the left, and the usual *symptoms* consist of severe pain in the testis or groin followed by swelling and tenderness of the testicle. There is often nausea. The *causes* are (1) predisposing in the form of an unusually long spermatic cord or gubernaculum testis, roomy tunica vaginalis, undescended testis and poor anatomic attachment of the epididymis to the testicle, and (2) exciting, consisting of cough, sneeze, straining at stool, vigorous exercise or often no known exertion. In some cases, symptoms will pass off and the condition may or may not recur. In others, they persist and if one is to save the testicle immediate operation is mandatory.

tions from one to the other are frequent. (1) *Adult teratoma*, where ectodermal (squamous epithelium with its appendages and teeth), entodermal (respiratory and intestinal epithelium) and mesodermal (cartilage, bone, muscle and fat) elements are found in varying proportions. (2) *Solid*, which includes both the so-called seminoma and embryonal carcinoma. These tumors constitute the bulk of testicular growths. They appear as large sheets or columns of sharply defined, large or moderate in size, polyhedral or round uniform appearing cells (Fig. 360). The cytoplasm is usually of a

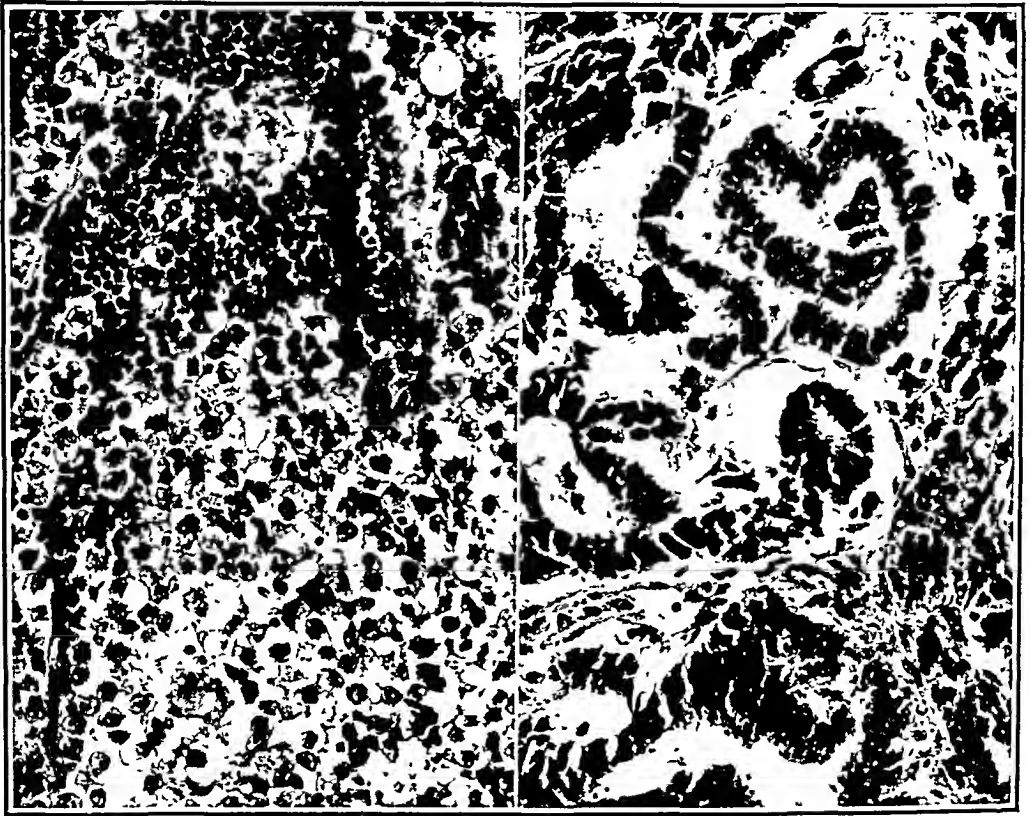


FIG 360

FIG 361.

FIG. 360.—Seminoma of the testis same case illustrated in figure 359 There are sheets of polyhedral cells with clear cytoplasm and uniform appearing nuclei. The stroma is scanty and contains lymphocytes x 100

FIG. 361.—Adenocarcinoma of the testicle showing well-formed glands lined with columnar epithelium. x 100.

poor quality, moderate in amount and clear although it may be dark and less abundant. The nuclei are central round or less often bizarre and disclose a central nucleolus and clumped chromatin. Neoplastic giant cells are sometimes found and, occasionally, there are foreign body giant cells. The stroma varies in amount but is usually scanty. It consists of granulation of fibrotic connective tissue and contains lymphocytes, plasma cells or eosinophils. (3) *Adenocarcinoma*, wherein the tumor is arranged in acini (Fig. 361). They are lined with cuboidal or columnar epithelial cells, often show papillary infoldings, have lost their polarity, vary in size and reveal hyperchromatic nuclei. (4) *Chorioepithelioma*.

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SCROTUM

ANATOMY

The scrotum is a cutaneous pouch, placed below the symphysis pubis, that contains the testes. It is divided into a right and left part by the *raphe* which continues to the under surface of the penis and in the opposite direction along the perineum to the anus. The left side hangs lower than the right. The external surface is composed of thin, brown corrugated *skin* that contains thin hairs and sebaceous glands. Beneath the skin is the *dartos tunica*—a thin layer of smooth muscle that is continuous with the superficial fascia of the groin and perineum. It is closely adherent to the skin, but is connected by delicate areolar tissue to the underlying fascias. The *arteries* consist of the external pudendal branches of the femoral artery, the scrotal branches of the perineal and the cremasteric branches of the inferior epigastric. The *lymphatics* drain into the inguinal nodes. The *nerves* are derived from the lumbar plexus, the perineal nerves and the posterior femoral cutaneous nerves.

PATHOLOGY

Since the scrotum is part of the skin it is subject to most of the cutaneous lesions already described in Chapter I. It is sufficient here to enumerate only the more common disorders.

Congenital Anomalies.—These are few. The scrotum may be *hypoplastic* in cases where the testes fail to descend or, having descended, where they fail to develop. *Hyperplasia* or redundancy sometimes occurs. *Bifid scrotum* is perhaps the most important, for with such it may be difficult to decide whether the patient is a male or a female. The lesion may be found with otherwise normal external genitals or the penis may be rudimentary and the urethra may open into the perineum.

Inflammations.—These are varied and many. Of particular interest are: *epidermophytosis*—occurring in the inguinal folds and similar to corresponding lesions of the feet (athlete's foot); *intertrigo*—an infection caused by the yeast-like fungus *monilia* and other organisms that occur in the natural folds. It is aggravated by perspiration and is more common in diabetics; *pediculosis pubis*—a parasitic infestation of the outer layers of the skin and its surface accompanied by profound itching; *gangrene*—already considered in conjunction with the penis; *furunculosis*—infection of hair follicles and sebaceous glands similar to that in the skin; *granuloma inguinale* and *lymphopathia venereum* both of which have been described in Chapter XIII; *actinomycosis*—identical to similar lesions elsewhere and *syphilis*—in the primary, secondary or tertiary stages.

Tumors.—Among others the following tumors of the scrotum have been described: from the epidermis and appendages, a papilloma, sebaceous cyst and carcinoma; from midline epithelial inclusions, an epidermoid cyst; from blood vessels, a hemangioma; from pigment producing cells probably of nerve tissue origin, a pig-

mented nevus, from fat tissue, a lipoma, from mesodermal elements is a result of metaplasia, a chondroma and osteoma, and also from mesodermal tissue, a "sarcoma" Of these the carcinoma is the most common In the past it has been associated with coal tar workers and "chimney-sweeps" It exists as a nodule that ulcerates or as a papillomatous mass Histologically, the growth is usually a well differentiated squamous cell carcinoma It remains localized for a long time, but ultimately metastasizes to the inguinal lymph nodes and elsewhere

Mechanical Disturbances—In the wall of the scrotum these include *traumatic avulsion* of the skin which was included in the section on the penis, *contusions* These result in extensive hematomas because of the laxity of the subepithelial tissue, *lacerations* which, as a rule, bleed freely and profusely, and *edema* which may be the result of a systemic disease as cardiac failure or glomerulonephritis or it may be the result of local conditions such as filariasis

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Chapter XIX

FEMALE GENITAL SYSTEM

EMBRYOLOGY

THE development of the internal sex organs to the point where the gonads begin to differentiate has been traced in Chapter XVIII. In the eighth week, the internal epithelial mass forms an outer more dense cortex and an inner less dense medulla. From the latter, a cellular mass bulges into the mesovarium to produce the rete ovium. By the fourth month, most of the cells of the internal cell mass produce ova, while proliferation of others together with proliferation of germinal epithelium results in a new cortex. At the same time, connective tissue from the rete extends into the ovary and near the periphery produces the tunica albuginea. Also with the appearance of the new cortex, the ova in the medulla disappear whereas those at the periphery remain and later produce the *Graafian follicles*.

The rete ovium is vestigial but canalizes and often connects with the mesonephric tubules. The cranial tubules are rudimentary, remain attached to segments of the mesonephric ducts, and together constitute the *epoophoron*. Some of the tubules of the *epoophoron* near the fimbriated end of the tube are called vesicular appendages. The more caudal mesonephric tubules remain as the *paroophoron*. Most of the mesonephric ducts (originally Wolffian ducts) disappear, but segments may persist at any level between the *epoophoron* and the hymen. They are located on the wall of the uterus or on the vagina and are known as *Gartner's ducts*.

With the development of the adrenals and kidneys, the proximal portions of the Mullerian ducts are pushed laterally and remain separate as the *fallopian tubes*. The intermediate portion of each tube unites with its fellow to produce the uterus proper, while the distal portions also unite to produce the *ovary* and the upper part of the *vagina*. The lower portion of the *vagina* develops from entodermal epithelium of the urogenital sinus which invades this area. The *hymen* arises from the genital cord and separates the *vagina* from the outlet of the urogenital sinus, which later becomes the *vestibule*. The fallopian tubes and uterus are lined by a simple epithelium. In the uterus, this develops glands at about the fourth month. The *vagina* is a solid mass of epithelium until about five months, when a cleft appears. The muscle of the entire tract makes its appearance as a condensation of mesenchyme at about the third month of embryonic development.

In the female, the phallus remains rudimentary as the *clitoris*. The urethral groove does not extend to the glans as in the male but remains as the *vestibule*, and the urethral folds, instead of uniting, remain free as the *labia minora*. The labio-scrotal swellings unite only posteriorly in front of the anus to produce the posterior commissure while laterally they remain as the *labia majora*.

VULVA

ANATOMY

The external genitals of the female are known as the vulva or pudendum. They consist of: (1) *Mons pubis*—a rounded eminence in front of the pubic bone produced by a subcutaneous collection of fat. (2) *Labia majora*—two folds extending posteriorly from the mons pubis and separated by a cleft. They unite anteriorly to form the anterior commissure and posteriorly to form the posterior commissure. (3) *Labia minora*—two folds extending posteriorly from the clitoris between the labia majora and the orifice of the vagina. In the virgin, the posterior ends of the labia minora are united to form the fourchette. The anterior ends split around the clitoris to form the prepuce above and the frenulum below. (4) *Vestibule*—cleft between the labia minora containing the openings of the vagina, urethra and Bartholin's (vestibular) glands. (5) *Clitoris*—the homologue of the penis. It is located posterior to the anterior labial commissure, is encircled by the split anterior ends of the labia minora, is covered by a glans, and consists of two corpora cavernosa whose crura are attached to the pubic bones. (6) *External urethral orifice* located 2.5 cm. posterior to the glans clitoris. (7) *Hymen*—thin fold of mucous membrane medial to the labia minora and at the lower end of the vagina. After rupture, its place is indicated by rounded elevations called carunculae. (8) *Vaginal orifice*—a median slit below the urethra and bounded by the hymen. (9) *Bartholin's (vestibular) glands*—the homologues of Cowper's glands in the male. They consist of two bodies situated on each side of the vaginal orifice posteriorly. Each drains by a duct that opens between the hymen and labium minus.

Histologically, the *labia majora* are covered with epidermis which contains hair on the outer surface and on both surfaces numerous sebaceous and sweat glands. Beneath the epidermis there are smooth muscle, fat and connective tissue. *Labia minora* are covered by squamous epithelium and contain connective and elastic tissue and sebaceous glands. The *clitoris* is covered with squamous epithelium and centrally consists of erectile tissue. *Bartholin's glands* are of the tubulo-alveolar type. They are lined with cuboidal or columnar epithelium with basilar nuclei. Most of the duct is lined by a stratified columnar or transitional epithelium except at the orifice where it is of a squamous variety.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the vulva consist of (1) *hypoplasia*, (2) *hyperplasia*, (3) *duplication*, (4) *absence* of mons pubis and (5) *synechia*. These are fine or more dense adhesions that are formed between the free edges of the labia minora. It is not settled whether they are congenital or acquired. They usually produce no symptoms unless they encroach upon or

cover the urethra when they cause deflection or interruption of the stream and infection of the urinary tract

Inflammations—Being composed essentially of skin the vulva is subject to most of the cutaneous infections found elsewhere on the body. The more important lesions may be listed as follows: (1) *Gonorrhea* (2) *Chancroid*—considered in Chapter XIII (3) *Furuncle*—considered in Chapter I (4) *Scleroderma*—considered in Chapter IX (5) *Psoriasis*—described in Chapter I (6) *Intertrigo*—fissuring, ulceration and exudation in the natural folds due to monilia and other organisms. It is aggravated by warmth, moisture and friction and is prevalent in diabetics (7) *Tinea cruris*—epidermophytosis or athlete's foot differing only in that it occurs in the inguinal region and pubis. It consists of red maculopapules that coalesce and becomes dry, scaly and fissured. They are attended by considerable itching (8) *Lichenification*—a non-specific process due to long continued scratching and rubbing. The skin is dry, swollen and indurated. The natural folds are deepened and the surface is pink, red or grey (9) *Kraurosis*—atrophy of the vulva. This is usually found after the menopause or in castrates and is due to suppression of ovarian activity. The surface is smooth, dry, usually gray or white, and parchment-like. Histologically, there is little or no keratosis, the epithelium is thinned, the rete pegs are atrophic, and the upper portion of the dermis is transformed into a band of dense fibrous tissue. There is no noteworthy inflammatory cell infiltration. Some authors class this as a separate disease, whereas others say it is the end stage of leukoplakia (10) *Leukoplakia*—in other sections of the book this has been included under tumors not because it is a neoplasm but because it is prone to become cancerous. In the vulva as elsewhere, there can be little doubt of such a transformation. Early, the area is red and swollen, then it becomes white, thick and retracted and finally it becomes deeply fissured. Histologically, there are hyperkeratosis, acanthosis, hypertrophy of the rete pegs, deepening of the papillae and a diffuse infiltration of the upper layers of the dermis with plasma cells and lymphocytes (11) *Granuloma inguinale*—considered in Chapter XIII (12) *Lymphopathia venereum*—also considered in Chapter XIII (13) *Syphilis*. This infection may affect the vulva in the primary, secondary or tertiary stages. The lesions are similar to those of the anus which have already been described in Chapter XIII. In decreasing order of frequency, the chancre is found on the posterior commissure (fourchette), labia majora, labia minora, urethra, perineum, vagina, thigh and mons pubis. Secondary lesions—*condyloma latum*—are found on the vulva, perineum, perianal region and the thighs. Tertiary lesions consist of gummas and are rare. The histologic changes in syphilis have been described in Chapter I (14) *Tuberculosis*. The vulva is affected in about 2 per cent of all cases of tuberculosis of the female genital tract. In most instances the route of infection is by the blood stream or lymphatics from other foci in the body. Rarely, it is said to be primary and contracted from infected ejaculates in cases where the male has genital tuberculosis. The lesion starts as a small nodule

that breaks down, discharges and leaves a punched out irregular ulcer with undermined edges and a grey necrotic floor and base. The diagnosis can be made with certainty only by biopsy.

Gonorrhea is of course caused by *neisseria gonorrhoeae*. It is contracted by intimate contact with pus that contains the organisms. In adults this usually occurs as a result of intercourse, whereas in infants and children the transfer of organism is ordinarily by contaminated objects such as linen, instruments, fingers and, rarely, toilet seats. A predisposing factor in infants and children is said to be the lack of cornification of the epithelium of the vulva and vagina. In adults, the epithelium is well keratinized and the mucosa is, therefore, more resistant. In contrast, however, Skene's ducts of the urethra, Bartholin's glands and the cervical glands are well developed in adults and it is in these areas that the organisms become hidden and periodically reinfect the patient.

From the surgical point of view, the two important sites of infection are the cervix and *Bartholin's glands*. In the acute stages, the latter become swollen, distended, red, painful and exquisitely tender. When the duct becomes sealed off, as it so often does, there is formed a frank *abscess*. This is filled with thick creamy pus that contains numerous neutrophils. In these are found the causative organisms. Histologically, the wall reveals a non-specific acute inflammation with varying degrees of necrosis. When the infection is less virulent or when the duct remains patent the process sooner or later becomes *chronic* and is then unattended by any symptoms except in the periods of exacerbation. In such cases, the epithelium of the ducts may remain normal or be transformed to a stratified squamous cell type; the glands may become hyperplastic or destroyed, and throughout there is fibrosis and infiltration with plasma cells, lymphocytes and monocytes. In cases where the duct is occluded and the infection is mild or burns itself out, the secretions of the gland accumulate to form a *cyst*. Although variable in size, a Bartholin's cyst usually measures less than 5 cm. in diameter. The lining is composed of flattened or tall transitional cells, squamous cells, columnar cells or cuboidal cells and in the subjacent connective tissue there are almost always remnants of the tubulo-alveolar glands. Before leaving the question of Bartholinitis, it ought to be pointed out that all cases are not caused by *neisseria gonorrhoeae* and that any organisms may be responsible for the infection.

Tumors.—Histogenetically, neoplasms of the vulva that have been described may be classified as follows: from the epithelium, papillomata (condyloma acuminatum) Bowen's disease, and carcinoma; from sebaceous glands, a cyst; from sweat glands, a hydradenoma, hydradenoid carcinoma, and Paget's disease; from Bartholin's glands (epithelium), a cyst and carcinoma; from pigment producing cells (melanoblasts), a nevus and melanoblastoma; from connective tissue, a fibroma and fibrosarcoma; from vessels, a hemangioma, lymphangioma and hemangiosarcoma; from fat, a lipoma; from nerve tissue, a neurofibroma, ganglioneuroma and neuroma; from muscle, a leiomyoma; from lymphoid tissue

(reticulum cells), lymphoblastomas, from mesodermal tissue as a result of metaplasia, a chondroma, of congenital origin, accessory breast, and from distant areas, metastatic tumors including chorionepithelioma and endometriosis. Since most of these tumors have been described in detail in Chapter I and other sections of the text they will not be dealt with further. Carcinoma alone merits separate consideration.

Carcinoma of the vulva is said to constitute about 4 per cent of all cancers of the female genital tract. Although its precise cause is unknown, leukoplakia has been reported as a precursor in from one-third to one-half of all cases. The lesion is seen from the third to the ninth decade of life with the majority of patients around sixty years of age. Symptoms consist of a lump or ulcer in about one-third of all cases together with combinations of pruritus, pain,



FIG. 362.—Fungating carcinoma of the vulva. (Courtesy Dr. Lewis C. Sheffield.)

bleeding, leukorrhea, and burning and frequency on urination. In decreasing order of frequency, the sites of the cancer are labia majora, labia minora, clitoris, urethral meatus, posterior commissure and Bartholin's glands. Grossly, as already stated, the lesion frequently starts in a leukoplakic plaque. It may be a small nodule that soon ulcerates or it may be primarily an ulcer. As the growth progresses it becomes essentially a large, fungating, superficially or deeply fissured, firm, ulcerating, grey, pedunculated or sessile cauliflower-like mass or an infiltrating, penetrating sloughing ulcer (Fig. 362). The edges of the latter are raised, firm and ill-defined, the floor is covered with necrotic material, and the base is composed of greyish white firm tumor that infiltrates and destroys all underlying structures. Histologically, about 90 per cent of the growths are squamous cell carcinomas and the remainder are adenocarcinoma, basal cell carcinoma and rarely Paget's disease. These are in every respect identical to similar growths in other areas of the skin.

Spread of the tumor is slow, is usually by way of the lymphatics, and affects the inguinal, deep femoral and iliac nodes. Because of the free anastomosis of vulval lymphatic channels, metastases are often bilateral. Microscopically detected tumor has been reported in 30 per cent of nodes that were not enlarged clinically. *Early diagnosis* can be established with certainty only by biopsy. *Treatment* is complete vulvectomy with bilateral dissection of the draining lymph nodes. The five year survival rate is about 25 per cent.

Mechanical Disturbances.—These consist of: (1) *trauma* which may be caused by external violence or more commonly is associated with delivery. The latter exists in the form of tears usually through the posterior commissure towards or into the rectum. More desirable are surgical incisions in the same area known as episiotomies; (2) *hematoma*—an accumulation of blood in the submucosal tissues. As a rule, it appears six to ten hours following spontaneous or operative delivery and it affects one labium majus. Its cause is rupture of a vessel or failure to secure hemostasis in an episiotomy. It may be associated with intense pain and swelling or, if bleeding also occurs internally, with signs of acute blood loss and anemia. The patient may die from shock or the hematoma may become infected and result in an abscess. Usually the extravasation is small and is resorbed spontaneously or is readily amendable to simple incision, evacuation of clots and ligation of bleeding points; (3) *edema*—most often associated with anasarca of cardiac failure or renal disease, particularly at the time of pregnancy. Less often it results from obstruction to the portal circulation from hepatic disease or pressure by a tumor. Local causes are those which interfere with local venous or lymphatic drainage. Chief among these are lymphopathia venereum and filariasis. The latter, known as *elephantiasis*, is frequently associated with massive swelling, thickening of the skin, hypertrophy of the epithelium, edema of connective tissue, increase of lymphatics, and diffuse non-specific inflammation. In addition, the zones around the parasites disclose typical granulomatous lesions which have already been described in connection with the lymph nodes; (4) *superficial atresia*. Atresia has already been considered under synechia of the labia minora. It occurs most frequently in infants and young children, but it has also been described in women in the tenth decade of life. In these as in infants, symptoms consist of urinary obstruction and infection. Because of the lightness of the adhesions, separation of the labia is easy.

VAGINA

ANATOMY

The vagina is a canal situated between the vestibule and uterus and the rectum and bladder. Ordinarily, its walls are in apposition and on transverse section the structure assumes an H position. Its anterior wall is 7.5 cm. long and its posterior wall measures 9 cm. in length. The anterior wall is related to the bladder and urethra; the posterior wall overlies the perineal body, the anal canal, the

rectum and in its upper portion a reflection of the peritoneum, the lateral borders are in contact with the levator ani muscles, and the terminal portions of the ureters course close to the lateral fornices and then anterior to the vagina. The arterial supply comes from the vaginal, uterine, internal pudendal and middle hemorrhoidal branches of the hypogastric vessels. The veins after forming an external plexus drain into the hypogastric veins. The lymphatics empty into the external iliac, hypogastric and sacral lymph nodes. The nerves arise in the vaginal plexus and the upper sacral nerves.

Histologically, the vagina from within out consists of (1) *Epithelium* of a stratified squamous variety. Normally, the superficial cells show little or no keratinization but they do contain fat and glycogen. (2) *Lamina propria*. Beneath the epithelium this is loose, somewhat edematous and shows papillae, particularly in the posterior wall. The deeper portion is dense and contains a plexus of small veins. Throughout there are lymphocytes which sometimes aggregate to form small follicles. (3) *Muscular coat* consisting of a middle circular and an outer longitudinal layer of smooth muscle bundles. (4) An external *adventitial coat*. This consists of connective tissue and contains vessels and nerves.

Vaginal Smears—Although the vaginal epithelium responds to ovarian hormones, it is the consensus today that the changes are not precise enough to indicate the phase of the ovarian cycle. In smears made of vaginal secretions and stained by the Papanicolaou or Shorr method the following changes are noted: *postmenstrual stage*—numerous leukocytes and small green colored epithelial cells, *early estrogenic effect*—larger polyhedral squamous epithelial cells but still with a green color, *full estrogenic effect*—numerous fully cornified large polyhedral cells with small nuclei and abundant brilliantly orange colored cytoplasm together with a disappearance of leukocytes, *progesterone effect*—no reliable changes, *pregnancy*—epithelial cells elongated, concave or navicular with vacuolated cytoplasm and elongated or collapsed nuclei, and at the *menopause*—atrophic small round cells with lavender colored cytoplasm. Aside from these physiological changes, vaginal secretions (in cases with carcinoma of the cervix and uterus) also contain *neoplastic cells*. In carefully prepared and examined smears, exfoliated tumor cells may be found in as high as 90 per cent of these cases. In general, the criteria upon which a cytologic diagnosis of cancer is made are the same as those used in histologic work. Briefly they consist of an increase in size and irregularity of the cells, of a relative increase in size of the nucleus as compared with the cytoplasm, of alterations in the intensity of staining of the nucleus and of changes in size, number and prominence of the nucleoli. It cannot be over-emphasized, however, that in the study of vaginal secretions just as in the study of bronchial, prostatic and other secretions one must first become thoroughly familiar with the normal flora before one can hope to identify neoplastic cells. It must further be emphasized that both the flora, and to a lesser extent the neoplastic cells, differ with the system studied so that precise criteria must be established for each.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the vagina consist of (1) *atresia*—when recanalization of the solid stage is incomplete; (2) *septate*—ordinarily longitudinal and either partial or complete. The latter results in a double vagina. Rarely, there are encountered transverse septa or diaphragms; (3) *imperforate hymen*—This usually remains unnoticed until puberty when the products of menstruation are retained in the vagina and produce a pelvis mass; (4) *fistulas*—between the bladder or urethra and the vagina; (5) *absence*—Total lack of formation of the vagina is said to occur once in every 5000 births. In about one-quarter of the cases, there are associated anomalies of the urinary tract and in about one-fifth, there are hernias. The uterus and tubes are atrophic but the ovaries are normal. Approximately 50 per cent of the patients have no abdominal manifestations while the remainder disclose periodic cramps and pains that may be great enough to necessitate hysterectomy. Most of the patients are, in addition, affected adversely psychologically. Treatment consists of reconstructing a vagina with the aid of skin grafts. It is interesting to note that such epithelium will undergo the same cystic changes as does the normal vaginal mucosa; (6) *cysts*. These may be divided into congenital and *acquired*. The latter eventuate from sub-mucosal inclusions of epithelium sustained at the time of delivery or at the time of gynecological operations. The misplaced rests proliferate and degenerate to form cysts. The lining cells are stratified squamous and the contents are composed of greasy material similar to that found in sebaceous cysts. *Congenital* cysts eventuate from remnants of Gartner's (Wolffian or mesonephric) ducts. They may be single or multiple and unilateral or bilateral. They may occur anywhere along the course of the ducts and are, therefore, most commonly seen in the broad ligament, along the side of or laterally within the wall of the uterus, or in the vagina. Here they are always located along the antero-lateral wall. They vary in size up to 6 or 8 cm., have a smooth wall and are filled with clear fluid. The lining cells are ciliated or non-ciliated, cuboidal or cylindrical, transitional, or stratified squamous.

Inflammations.—Inflammatory lesions of the vagina are similar to many of those found in the vulva. They, therefore, need only be listed here: *gonorrhea*, *leukoplakia*, *granuloma inguinale*, *lymphopathia venereum*, *syphilis* and *tuberculosis*. Two more common lesions are simple ulcer and trichomoniasis.

Simple ulceration is observed in cases with foreign bodies, in prolapse of the uterus, in leukemias and in other debilitating conditions where the general resistance is low. The ulcers are usually small, multiple, superficial, irregular and clean. *Histologically*, they disclose a denudation of the epithelium and an infiltration of the underlying tissue with plasma cells, lymphocytes, monocytes and neutrophils.

Trichomoniasis in relation to the vagina means infestation with the *trichomonas vaginalis*. This is a pear shaped protozoan with

four anterior flagellae and a dorsal undulating membrane without a posterior free portion. Its size varies from 12 to 24 microns in length to 6 to 8 microns in diameter. The organism is found in from 16 to 37 per cent of gynecological patients and in 66 per cent of prostitutes. It produces a thin, bubbly, copious discharge that overflows and excoriates the perineum and vulva, and is attended by much itching. The vaginal mucosa is red, edematous, covered with pus and flecked with tiny grey ulcers. *Histologically*, these are non-specific. The diagnosis is established by demonstrating the parasite in smears of secretion obtained from the posterior wall of the cervix and vagina. The infection is tenacious. Some of the many drugs that have been used locally are stovarsol powder, floroquin tablets, sulfonamide ointments and vinegar douches.

Tumors—Neoplasms of the vagina are neither common nor varied. From the epithelium there may arise a papilloma and carcinoma, from connective tissue, a fibroma and myxoma, from muscle, a myoma, from pigment producing cells (melanoblasts), a nevus and melanoblastoma, from lymphoid tissue (reticulum cells), a lymphoblastoma, from mesodermal elements, sarcoma, and from distant areas, secondary tumors and endometriosis.

Carcinoma—Carcinoma of the vagina is rare. It may occur at all ages from infancy to senility but is most common in the fifth and sixth decades. *Early* there is a blood tinged leukorrhea, but as the lesion extends to adjacent structures and organs there are pain, rectal distress and urinary disturbances. The tumor may be localized to one area of the vagina (usually the posterior portion and upper half) or it may encircle the entire lumen. It grows as a fungating, cauliflower-like, friable mass or as an infiltrating, indurated ulcer. *Histologically*, it is usually of the squamous cell type, but, occasionally, it is of an adenomatous variety. *Spread* is by local extension to adjacent structures and only later by metastases to the iliac, hypogastric and sacral lymph nodes. *Treatment* is irradiation. The *prognosis* is poor for less than 15 per cent of patients are alive at the end of five years.

Sarcoma—Sarcoma of the vagina is also rare. It occurs as frequently in infants and young children (*sarcoma botryoides*) as it does in adults. A bloody vaginal discharge is the first symptom and later, as in carcinoma, there are pain and urinary and rectal manifestations. As a rule, the tumor not only fills the vagina, but it grows rapidly and soon fills the entire pelvis. In the literature, there has been practically no attempt to separate these tumors on a histogenetic basis. Although there undoubtedly occur fibrosarcomas, myosarcomas, myxosarcomas, neurofibrosarcomas, etc., most of the reports merely list them as spindle cell, round cell or mixed cell sarcoma. Also the often used designation of mucosal (protruding from the mucosa into the vagina) and parietal (originating and growing extramucosally) sarcoma has little to recommend it, for all sarcomas of the vagina must arise extramucosally, otherwise they would not be sarcomas. Irradiation therapy is the only treatment possible or desirable. Most of the patients die in from one to twenty-four months.

Mechanical Disturbances.—Mechanical disturbances of the vagina consist of the following: (1) *Rupture*. This may occur as a result of coitus or of insertion of a foreign object. In one patient observed by the author, the tear was produced by a broom handle. The victim was admitted to the hospital with most of the small intestine protruding from the vagina. She died from peritonitis following replacement of the gut. The immediate danger in rupture of a vagina is profuse hemorrhage. (2) *Vesicovaginal fistula*. Most fistulas between the bladder and vagina are acquired. One of the common causes in countries where midwifery is permitted is faulty labor. Prolonged pressure of the head on the soft parts, especially when the bladder is distended, produces ischemia, degeneration and necrosis. If then forceps should be used there is further trauma and even perforation. As a rule, however, leakage of urine does not start until the third or fourth postpartum day. Other causes of fistulas, which are more common in countries where obstetrical care is better, are extension and breakdown of carcinoma of either the cervix or the bladder, irradiation necrosis and total hysterectomy. (3) *Calculus*. Stones may form in the vagina or may reach this organ by eroding through the bladder. Primary calculi can form only in the presence of a congenital or an acquired vaginal stricture, added to which there is leakage of urine into the vagina either through a fistula or by way of incontinence. The size varies from a millimeter to 10 cm. or more and the composition is the same as that of urinary calculi. (4) *Foreign bodies*. These are found in the vagina because of accident (surgical material), curiosity (children), sexual perversion, feeble mindedness and insanity. The outstanding symptom is leukorrhea. The diagnosis is made by rectal, vaginal and roentgenographic examination. Treatment is removal. Some of the many objects which have been found in the vagina include the following: empty shells, grain, nuts, rolled up straw, cherry stones, sticks, potato, metal containers, hair pins, straight pins, safety pins, cork, paper, cotton, calcium oxalate crystals, shoe buttons, rubber balls, cap of tooth paste tube, screw, bottle, sandstone, tampons, pebbles, ox tongue, leeches and pessaries.

UTERUS

ANATOMY

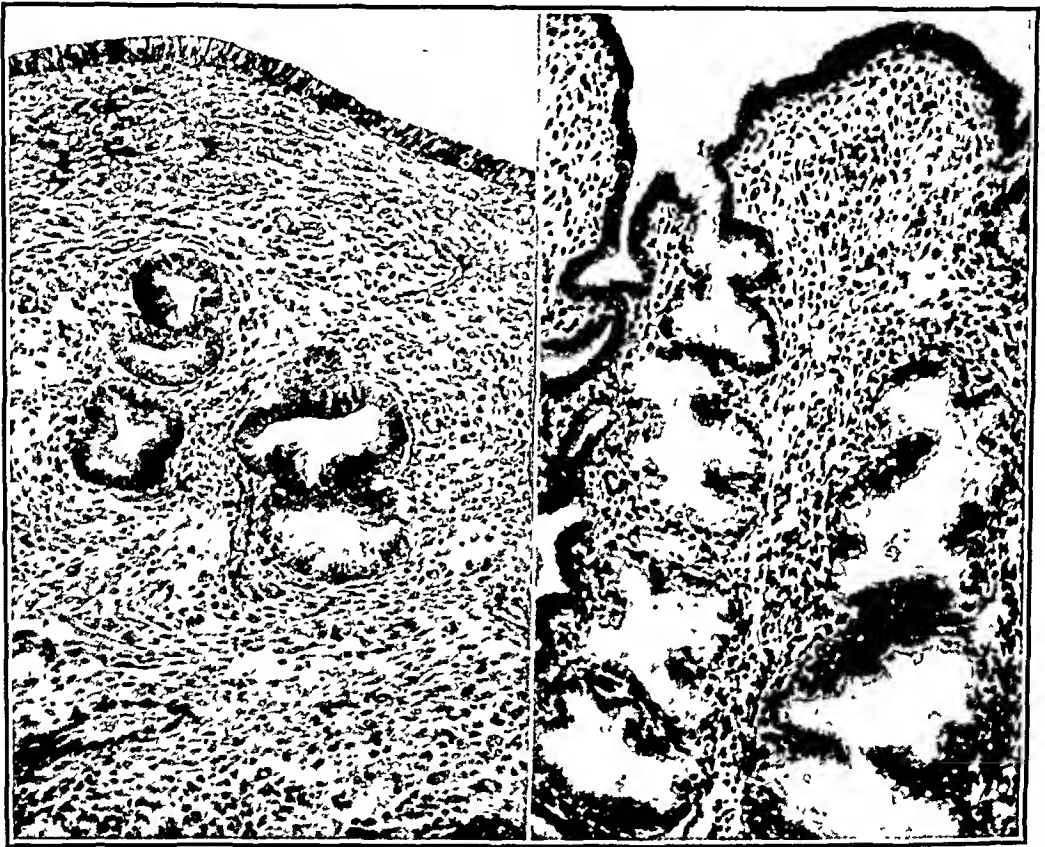
The uterus is located in the pelvis between the bladder anteriorly and the rectum posteriorly, and is connected with the fallopian tubes above and the vagina below. In the virgin, it has the shape of a flattened pear, measures approximately 7.5 x 5 x 2.5 cm., and weighs about 35 gm. Its long axis parallels the axis of the superior pelvic inlet and it forms an angle with the vagina. It consists of a body and a cervix which are separated by a slight constriction called an *isthmus*. The *body* narrows from the fundus to the isthmus. It is covered by peritoneum which anteriorly is reflected on to the bladder to form the *vesico-uterine pouch*, and posteriorly extends to the cervix from which it is reflected on to the rectum to form the

recto-uterine pouch (of Douglas) Its anterior surface is in apposition with the bladder and its posterior surface rests upon the pelvic colon and small intestine Attached to the lateral margins are the *broad ligaments* consisting of two folds of peritoneum and each containing superiorly the *fallopian tube*, inferiorly and anteriorly the *round ligament* and inferiorly and posteriorly the *ligament of the ovary* The lateral margin of the broad ligament is attached to the wall of the pelvis That part of the body of the uterus that lies above the level of the fallopian tubes is known as the *fundus* The *cervix* measures 2.5 cm in length Its long axis forms an angle with that of the uterus The portion above the vagina is separated from the bladder by cellular tissue known as *parametrium*, while posteriorly it is covered by peritoneum The vaginal portion projects into the vagina, and contains an aperture—the *external orifice* which is bounded by a short anterior lip and longer posterior lip The *uterine cavity* is triangular in shape and flat It communicates with the *cervical canal* by the *internal orifice* The arterial supply comes from the uterine branches of the hypogastric and the ovarian branches of the abdominal aorta The veins end in the uterine venous plexus The *lymphatics* of the cervix drain into the external iliac, the hypogastric and the common iliac nodes, while those of the body and fundus pass to the pre-aortic, external iliac and superficial inguinal nodes The nerves are derived from the hypogastric and ovarian plexus and the pelvic splanchnic nerves

Histologically, the wall of the body of the uterus consists of (1) a *serosa*—composed of an external layer of mesothelium resting upon a thin layer of loose connective tissue, (2) *myometrium*—composed of bundles of smooth muscle that are separated by interstitial connective tissue This contains isolated smooth muscle cells, reticulum, and in the outer portion elastic fibers, (3) *endometrium* This will be discussed separately The *cervix* is composed mainly of a stroma of connective tissue At its junction with the uterus, however, there are added smooth muscle fibers in increasing numbers The vaginal portion of the cervix is covered with *stratified squamous epithelium* that normally shows no keratinization At approximately the external os, there is an abrupt transition to a single layer of tall, non-ciliated, *columnar epithelium* Their nuclei are oval, deeply staining and basilar and the cytoplasm is neutral or slightly basophilic and is rich in mucin This epithelium lines the cervical canal to the internal orifice Along its course it sends numerous projections into the stroma which arborize to form *racemose cervical glands*

Endometrium — *Menstruation* is periodic bleeding from the uterine cavity normally occurring every twenty-five to thirty-five or on an average every twenty-eight days As a rule, it is of the ovulatory type but sometimes, especially at the menarche and the menopause, it may be of the anovulatory type At the risk of oversimplification the *hormonal control* of menstruation may be briefly outlined as follows The anterior lobe of the *pituitary* gland secretes two hormones that act upon the ovary—one causing stimulation and maturation of the ovum and the other bringing about lutini-

zation of the ruptured follicle. Thus after the end of menstrual flow, several follicles begin to mature and as they do so, they secrete increasing amounts of *estrogen* (estrogenic hormone, female sex hormone, folliculin, estrin or theelin as it is also called). For some unknown reason only one follicle reaches maturity and ruptures, whereas the rest degenerate. The remains of the follicle after the ovum has been discharged are transformed into a *corpus luteum* and this secretes some estrogen as well as another hormone, *progesterone*. Estrogen alone causes proliferation of endometrium, whereas estrogen plus progesterone promotes differentiation or



A

B

FIG 363.—Normal endometrium showing (A) proliferative and (B) secretory phase
x 50.

secretion and simultaneously inhibits ovulation. When the corpus luteum degenerates menstruation ensues.

The *proliferative phase* (first growth, follicular or interval phase) of the endometrium, therefore, corresponds to the ripening of the follicles and ends with ovulation. In a twenty-eight day cycle this occurs about fourteen days after the first day of the last menstrual period. After menstruation the endometrium consists of a thin basilar layer and only a portion of the next layer the spongiosa. The raw surface is soon covered with epithelium from the underlying glands. The latter are small, few in number, narrow, straight and are lined by columnar epithelium (Fig. 363A). The luminal and other surfaces of the cells are sharp; the cytoplasm is solid and

eosinophilic, and the nuclei are round or oval and basilar. The stroma is abundant dense and composed of spindle cells with deeply basophilic spindle nuclei. In the latter part of the proliferative phase the glands become more numerous, elongated and show beginning tortuosities. Their lining cells are slightly larger and the nuclei tend to leave the basilar portion. The stroma in the basilar portion remains dense, but that in the superficial portion is looser and the nuclei are larger and more vesicular. The vessels are small numerous and engorged.

The *secretory phase* (second growth, differentiative, pro gravid or progestational phase) of the endometrium corresponds to the corpus luteum activity of the ovary. It extends from the fourteenth to the twenty-sixth day of the cycle. The endometrium gradually increases to a depth of about 5 mm. The glands are numerous, are arranged in parallel rows at right angles to the surface and show increasing tortuosities (Fig 363B). Three layers are now discernable, (1) a *basilar* which is similar to that already described, (2) a *spongiosa*—composed of the most tortuous and dilated portions of the glands and (3) a *compacta* near the surface where the glands become straighter and narrower. The lining cells disclose sub-nuclear droplets of secretion and deposits of glycogen. Later, the cytoplasm becomes reticulated and watery. The luminal portion sloughs and becomes frayed and the glands are filled with secretion. The stroma undergoes a decidual transformation. The cells become larger and sharply defined. They are of varied shapes, send processes into the surrounding tissue, have eosinophilic cytoplasm and reveal large vesicular nuclei. There is considerable edema. These changes are most marked in the outer two layers.

The *ischemic phase* occurs one to two days before menstruation and is characterized by constriction of the spiral vessels that pass between the basilar and spongiosa layers. As a result, the superficial portion becomes blanched and ischemic, the endometrium shrinks due to loss of water, the stromal cells are dense, the glands collapse, and leukocytes appear.

The *menstrual phase* occurs as a result of hemorrhage consequent to degeneration, necrosis and breaking of the vascular walls. These changes are brought about by prolonged vascular constriction.

Anovulatory menstruation occurs when the follicle develops to maturity or beyond but instead of rupturing it dies and degenerates. The consequent sharp drop in estrogen production brings about menstruation. Histologic examination of the endometrium before menstruation shows normal or hyperplastic proliferative activity and lack of secretory changes.

PATHOLOGY

Congenital Anomalies—Developmental malformations of the uterus result from a faulty fusion of the Mullerian ducts. They may be listed as follows: *absence*—resulting from failure of the ducts to develop, *double*—complete failure of fusion. This may be

associated with a single or a double vagina; *two horns*—failure of fusion of the upper portions of the ducts; *notched*—when the upper line of fusion is indicated by a notching of the fundus, *one horn*—failure of one Mullerian duct to develop; *septate*—a longitudinal division of the uterine cavity by a partial or a complete septum, and *atresia of the cervix*.

Inflammations.—Inflammatory lesions of the cervix consist of non-specific cervicitis and, rarely, tuberculosis, syphilis and granuloma pyogenicum. Those of the endometrium consist of endometritis, pyometria, tuberculosis and rarely, granuloma inguinale.

Non-specific Cervicitis.—This is the commonest lesion of the female genital tract. Two factors are responsible for its frequency—the nature of the arborizing cervical glands which offer a nidus for organisms and repeated trauma, such as sustained at the time of delivery. Any of the pyogenic organisms may cause the infection. The more common are streptococci, staphylococci and gonococci. In the *acute stages*, the cervix is red, swollen and covered with a purulent discharge. *Histologically*, the glands are filled with pus; the supporting connective tissue is edematous and contains engorged capillaries, and there is a diffuse infiltration with neutrophils.

Chronic Cervicitis.—This results from a persistence of the acute infection. It may be limited to the endocervix in which case the canal is granular, soft and often filled with a mucopurulent plug. More frequently, however, it extends on to the vaginal surface to produce an everted, red granular, protruding mass. The cervix is edematous and hypertrophied; its os is patulous; its lips are gaping, and its glands are occluded resulting in retention cysts (Nabothian) that measure as much as 2 cm. in diameter. They are filled with clear viscid fluid or pus. *Histologically*, the surface epithelium may be normal or partially or completely eroded. The glands are both hypertrophied and hyperplastic, and they show an excess of secretory activity. The surrounding tissue may be edematous and vascular or dense and sclerotic. There is a diffuse infiltration with plasma cells, lymphocytes, monocytes and neutrophils.

Both in the involved and in remote areas there is often a change of the covering columnar epithelium and of the glandular epithelium to a stratified squamous cell type. The older theory is that inflammatory irritation causes a proliferation of adjacent squamous epithelium which creeps along the basement membrane and elevates the pre-existing columnar cells. This process is called *epidermidization*. The newer and, I must say, rather cogent explanation is that squamous epithelial cells are produced locally from basal cells as a result of relative hyperestrinism. This process is referred to as *squamous metaplasia*. In either case, the lesion must be differentiated from squamous cell carcinoma. Ordinarily, the distinction is easy for the benign condition is limited to the surface or to the glands, shows an intact basement membrane, reveals no loss of polarity of the cells, and is devoid of the variations in shape size and staining qualities that always mark a carcinoma.

Endometritis—Non-granulomatous infection of the endometrium is almost always due to pyogenic organisms, the most common of which are streptococci, staphylococci and gonococci. Predisposing factors are postpartum state, abortion, tumors such as fibromyomas, polyps and cancers, and irradiation. In the *acute stages*, there are varying degrees of hyperemia, edema, neutrophilic infiltration, degeneration, necrosis and nuclear fragmentation. In the *chronic* form, there are infiltration with plasma cells, lymphocytes and monocytes, increase in thick and thin walled capillaries, and proliferation of fibroblasts and fibrocytes. An inflammation of the endometrium, as would be expected, usually involves varying proportions of the muscle layer, thereby producing *acute* and *chronic myometritis*. Histologically, the changes correspond to those in the endometrium.

Pyometrium—This is a collection of pus in the uterine cavity to as much as 600 cc. The exciting causes are bacteria, especially aerobic and anaerobic streptococci and staphylococci, and colon bacilli. The predisposing cause is a partial or complete occlusion of the cervical canal. This is brought about by (1) congenital atresia, (2) inflammations either acute or chronic, (3) neoplasms, such as cancer of the cervix or endometrium, polyps, fibromyomas, etc., and (4) mechanical disturbances, such as malposition, irradiation and chemical ulcers.

Syphilis—Syphilis of the cervix is recorded as occurring in from 9 to 44 per cent of cases with syphilitic infection. It exists in the form of (1) a *chancre* that is usually grafted upon a previous cervicitis. It frequently surrounds the external os completely, but it may also be found on the anterior or posterior lip alone. It exists as an uneroded ulceration or as a sharp, ulcerated, funnel-shaped sore with an attached pseudomembrane, (2) *secondary* macules, erosions, papules and ulcers and (3) an ulcerating *gumma*. The histologic changes are similar to those described in the section on the skin.

Tuberculosis—This is more common in the endometrium than in the cervix, and in each it is almost always secondary to infection of the fallopian tubes. There may or may not be a demonstrable pulmonary lesion. Tuberculous endometritis is responsible for about 10 per cent of all cases of sterility. The uterus is frequently hypoplastic. *Histologically*, only the outer portion of the endometrium is affected. Because the infection is sloughed each month with the menstrual flow, the tubercles are almost always of the solid type. Caseation is rare. The organisms are isolated by guinea pig inoculation and cultural methods.

Tumors—Neoplasms of the cervix and uterus proper are not extremely varied. The following more common lesions will be considered. (1) *Benign*—hyperplasia of the endometrium, endometiosis, polyps, hypertrophy of the myometrium, and fibromyoma. (2) *Malignant*—carcinoma of the cervix, carcinoma of the endometrium, sarcoma and mixed tumors. Other lesions worthy of mention are papilloma of the cervix, lipoma, melanoblastoma of the cervix, lymphoblastoma and rhabdomyosarcoma.

Hyperplasia of the endometrium occurs at all ages during the reproductive cycle, is more frequent after thirty-five years of age and is infrequent beyond the menopause. It is *caused* by long continued estrogenic stimulation in the absence of a balancing corpus luteum effect. By this method, the lesion can be produced at will in experimental animals. In humans during the child bearing age, the source of the estrogens is said to be a persistence of unruptured Graafian follicles, and during the post menopausal period, it is thought to be derived from the adrenal cortex. At any age, excessive amounts are produced by granulosa cells and theca cells tumors. *Grossly*, the endometrium is thick, velvety, grey or pinkish grey and often polypoid. Tiny hemorrhages are common and minute clear vesicles may be detectable on close inspection. *Histo-*



FIG 364.—Hyperplasia of the endometrium showing large cysts some of which are filled with secretion. x 50

logic changes vary in degree from almost normal proliferative endometrium to one that is difficult to differentiate from carcinoma (Fig. 364). The following characteristics are observed: glands increased in number, irregularly arranged, and of varied shape and size from straight, serpigenous, bizarre to cystically dilated (Swiss cheese appearance); epithelium closely packed, deeply stained, moderate number of mitoses, cell borders distinct and usually sharp, cells one or more layers thick, cytoplasm, as a rule, devoid of glycogen droplets, nuclei oval or wedge shaped and hyperchromatic; stroma moderate in amount or scanty, dense or edematous, and often rich in vessels, and occasionally, small foci of necrosis. The chief *symptom* is irregular vaginal bleeding. The *diagnosis* is made by endometrial biopsy. *Treatment* consists of administration of anterior pituitary luteinizing hormone, of curettage, of radiotherapy and of hysterectomy.

Endometriosis may be defined as the presence of endometrial tissue in abnormal locations. There are three theories to explain its origin: (1) reflux from the uterine canal by way of the fallopian tubes at the time of menstruation, (2) a metaplasia of mesodermal tissue and (3) proliferation of misplaced Mullerian duct tissue. The lesions are spoken of as endometriosis interna (also adenomyosis and adenomyoma) when they affect the uterus and endometriosis externa when they affect other tissues. The latter include ovary, rectosigmoid, fallopian tubes, any of the other pelvic serosal and less often abdominal peritoneal surfaces, umbilicus, groin, thighs, vagina, cervix, vulva, abdominal and mediastinal lymph nodes and possibly the lungs. With such a wide distribution, signs and symptoms as would be expected are extremely variable. Periodic pain, swelling and tenderness apply generally. Increasing dysmenorrhea is the chief manifestation as far as the pelvic organs are



FIG. 365.—Endometriosis of a right ovary and fallopian tube

concerned. Grossly, the lesions appear as small or larger, cystic deep blue to almost black nodules, or cysts of varying sizes that are filled with old blood and that are surrounded by an abundance of fibrous tissue (Fig. 365). Histologically, the amount of glandular to stromal tissue varies so that at times diligent search may be necessary to find one or the other. Although sometimes the same cyclic changes are noted as in the endometrium proper, it is more common to encounter proliferative changes alone. The diagnosis is usually established from a history of recurrent symptoms associated with menstruation. Treatment consists of surgical excision or of artificial or natural castration. The prognosis with regards to life is good.

Polyps are pedunculated growths measuring from a few millimeters to several centimeters in diameter that arise in the cervix or in the endometrial cavity. It is a poor term unless further qualified, for although it is usually used to connote a finger-like mass composed

essentially of benign epithelium, yet a carcinoma, sarcoma and fibromyoma may present the same appearance. In this section, reference is made to the benign epithelial type of proliferation.

Cervical polyps are single or multiple, red, soft, friable, bleed readily upon manipulation and are usually attached by a thin pedicle. Depending upon the site of origin, they are covered by stratified squamous or tall secreting columnar epithelium. The latter, when present is directly continuous with centrally located large or small racemose glands that are lined by similar cells. Sometimes the glands are dilated to form cystic spaces. The stroma is variable in amount, dense or edematous, vascular and frequently infiltrated with plasma cells, lymphocytes and neutrophils. Often the surface is ulcerated, and in these or other areas the glandular epithelium is replaced with a stratified squamous cell variety. A cancerous transformation, however, is rare. *Symptoms* consist of bleeding, leukorrhea and sterility. *Treatment* is removal.

Endometrial polyps grossly are similar to those in the cervix. They arise anywhere in the endometrium and when they become large enough, they protrude through the cervix. The exposed vaginal surface may thus be ulcerated and covered with pus. *Histologically*, some polyps respond to ovarian stimuli just as does normal endometrium and one may encounter proliferative or secretory changes. Others, however, reveal only a hyperplastic proliferative epithelium with, frequently, a typical Swiss cheese-like pattern. There may or may not be an associated inflammation. Cancerous transformation is infrequent but does occur. *Symptoms* are absent in cases with smaller growths, but in others they are similar to those associated with cervical polyps. *Treatment* is removal.

Hypertrophy of the myometrium has also been called *fibrosis uteri*. From the pathologic point of view it is a disappointing lesion for the only deviations from the normal are a gross increase in thickness of the myometrium to about twice the usual size, a histologic increase in width of the muscle fibers and, as revealed by special staining, an increase of fibrous tissue particularly in the submucosal portion of the myometrium. The vessels are not altered. *Clinically* the lesion is seen in multiparous women between the ages of thirty-five to fifty years and is attended by prolonged menstrual and intermenstrual bleeding. The *cause* of the latter remains obscure.

Fibromyoma has also been called fibroid, fibroma, myoma and leiomyoma depending upon the author's concept of the relative amount of fibrous and muscle tissue within the tumor. Although the question as to the *cause* of fibromyoma is not yet completely settled, there are indications that it is due to prolonged continued estrogen stimulation in the absence of a balancing effect of progesterone. The lesion has been produced in spayed and normal animals by continued small doses of estrogens, while the addition of progesterone or testosterone propionate has had an inhibitory effect. Fibromyomas are most frequent between the ages of thirty and fifty years. *Symptoms* may be entirely lacking or they may, among others, consist of a dull or sharp pain, dysmenorrhea, menorrhagia and leukorrhea and there may be anemia and sterility.

Grossly, the tumors vary in number from one to many and in size from a millimeter to 40 or 50 cm in diameter. They may be located beneath the endometrium (submucosal), within the wall (intramural) and beneath the serosa (subserosal) (Fig 366). As they increase in size they produce marked distortion of the uterus and uterine cavity, so that in the laboratory, orientation is frequently difficult. Externally the tumor is rounded and in the submucous and subserous variety it may be pedunculated. It is stony hard to palpation, cuts with some difficulty, and the cut surface always bulges above the level of the surrounding tissue. It does not possess a true capsule, but the compressed adjacent myometrium renders an



FIG. 366.—Fibromyomata of the uterus located submucosally, intramurally and subserosally.

encapsulated appearance. When uncomplicated the tumor is grey or greyish white, solid and is composed of interlacing bundles or whorls. *Histologically*, it consists of ill-defined long spindle cells that maintain the criss-cross or spiral appearance seen macroscopically. The cytoplasm is eosinophilic and varies in amount from scanty to abundant. The nuclei are oval or spindle shaped, relatively scanty or abundant, sharply defined and evenly and lightly stained.

Deviations from the above standard pattern are so common that many of them can scarcely be called complications. Among these are (1) *hyaline change* indicated grossly by a replacement of the trabeculated and whorled appearance with homogeneous grey tissue

Histologically, varying proportions of the tumor are transformed into a solid mass of non-granular eosinophilic material. (2) *Red degeneration*. This represents a hemorrhagic infarct of a hyalinized fibromyoma in which the extravasated erythrocytes have been laked. (3) *Cystic* change which is usually associated with degeneration. The cysts may be small or replace most of the mass. (4) *Calcification* which may occur in tiny foci or may be widespread to involve the entire growth. (5) *Necrosis* and *gangrene* particularly in pedunculated tumors that have twisted on their pedicles. (6) *Infection*—extremely rare. (7) *Sarcomatous* change considered in the section on sarcoma. Of the many associated pathologic conditions, *carcinoma* of the endometrium is the most important. It occurs more frequently in uteri with fibromyomas than in those without.

The *diagnosis* of fibromyoma may be difficult or impossible when the growth is small, but as it increases in size the tumor is readily palpated. It may, however, be confused with any other neoplasm in adjacent organs. *Treatment* consists of myomectomy, hysterectomy or irradiation. Hormonal therapy (testosterone propionate or progesterone) has also been used but has little to recommend it. Ordinarily, the *prognosis* is good.

Carcinoma of the cervix is about six times as common as carcinoma of the endometrium. Its *cause* as in other organs of the body is not known, but it is thought that estrogens play a decisive rôle. Such injections in mice have resulted in the production of cervical cancer. Also by cornification counts in vaginal smears, it has been shown that the cervix contains a greater concentration of estrogens than does the vagina. Direct proof of its action, however, is lacking. Carcinoma of the cervix occurs at all ages but is most common from the fourth to the sixth decades. It affects multiparous women in over 90 per cent of the cases and is infrequent in Jews. *Symptoms* may occur early in some cases but appear late in others. The earliest detectable manifestations are painless bleeding or spotting between periods or postmenopausally and leukorrhea. The presence of pain or symptoms referable to the urinary or intestinal tract are late and indicate a hopeless situation.

Grossly, in the early stages, the cervix may appear entirely normal or it may present the usual changes characteristic of cervicitis. Lesions that clinically arouse suspicion of carcinoma are those in which there is granularity in a previous laceration, small ulceration covered with granular tissue and surrounded by firm tissue, or granularity and induration of the margin of the external os. All of these bleed readily upon manipulation. Henceforth the growth proceeds in one of the three directions: (1) *rapidly infiltrating* producing little visual distortion of the cervix and only slight or superficial ulceration. To palpation the entire involved area is often stony hard in consistency. (2) *ulcerating* and infiltrating—similar to the above except that in addition to the local extension there is concomitant ulceration and excavation of the surface. The tumor is hard, bleeds easily upon manipulation and may result in recto-vaginal or vesico-vaginal fistulas, and (3) *papillary* or

cauliflower-like, wherein there is slight or moderate extension into the surrounding tissue with the bulk of the tumor growing into the vaginal lumen (Fig 367). Such tumors are grey, friable and also bleed easily. *Histologically*, more than 90 per cent of cervical cancers are of the squamous cell variety. As such, they present the usual characteristics that have been described in connection with carcinoma of the skin. At one extreme there is the carcinoma in situ, where the epithelium is not thickened greatly and its basement membrane not broken but where the cells are irregular and bizarre



FIG 367—Infiltrating carcinoma of the cervix

Intermediary types are those which infiltrate the subjacent tissue but where the cells are well or moderately well-differentiated and can be recognized as of the squamous cell type. They may or may not show keratinization. At the other extreme are round, oval or irregular cells that diffusely penetrate all structures and may be difficult to distinguish from sarcoma. Most of the remaining 10 per cent of the cases are of the adenomatous variety (the usual type seen in the first two decades of life) while a few are of the basal cell variety. Spread of cancer of the cervix occurs (1) by direct extension to the parametrium, vagina, bladder, ureters and rectum, (2) by lymphatics to the iliac and hypogastric nodes and (3) by the blood stream to the liver, pancreas, lungs, bones, brain and other organs.

A *diagnosis* of carcinoma of the cervix is made from a history of intermenstrual bleeding, from a thorough inspection of the cervix, from an examination of vaginal secretions for neoplastic cells and from a biopsy. *Treatment* of choice is irradiation, although some clinicians in selected cases remove the entire uterus, adnexa and draining lymph nodes surgically. The *prognosis* is much better in early than in advanced cases and is also better in the fungating than the infiltrating type. The over-all five year survival rate is reported as ranging from 14 to 35 per cent.

Carcinoma of the endometrium is about one sixth as frequent as carcinoma of the cervix. Both account for about 16,000 deaths a year in the United States. Indications are that at least two *factors* are *responsible* for cancer of the body of the uterus, (1) a genetic



FIG. 368 —Fungating carcinoma of the endometrium

predisposition and (2) prolonged estrogenic stimulation. Evidence for the latter may be listed as follows: women who develop uterine cancer reach the menopause about six years later than normal; they are prone to excessive or irregular bleeding during the menopause at which time the endometrium is hyperplastic (estrogenic effect); cancer of the endometrium is frequently preceded by or is associated with hyperplasia, and granulosa cell and theca cells tumors of the ovary which are known to excrete estrogens are usually associated with hyperplasia and frequently, with carcinoma of the endometrium. Cancer of the body of the uterus is found in women of an average age of fifty-seven years, is rare before the age of thirty years and, in nulliparous, is more common than is cancer of the cervix. *Symptoms* before the menopause consist of menorrhagia, while after the menopause they consist of vaginal staining or spotting

in 95 per cent of the cases *Leukorrhea* is present in about 60 per cent of the cases

Grossly, the cancer may start in any portion of the endometrium as a small, raised, grey, friable and moderately firm nodule, or it may appear as a diffuse finely polypoid thickening of a portion or most of the endometrium that is difficult to distinguish from hyperplasia. As the lesion progresses the former is transformed into a large polypoid, grey, necrotic, friable mass that distends the uterine cavity and that is usually attached to the myometrium by a broad base (Fig 368). The diffuse variety merely becomes thicker, superficially necrotic and ulcerated. Each remains localized to the superficial layers of the myometrium for long periods of time and only late does it penetrate the wall to the serosa. Histologically, most of the lesions are adenocarcinomas that vary greatly in their degree of differentiation. At one extreme, the tissue may be difficult to differentiate from hyperplasia and, at the other, it may resemble a sarcoma. The majority are in between (Fig 369).



FIG 369—Well-differentiated adenocarcinoma of the endometrium showing a piling up of the epithelial cells, a loss of normal polarity and irregularity within the cells $\times 100$

In bona fide cases, the following features are usually encountered: increase in number of glands and decrease in stroma so that the acini are frequently in juxtaposition with each other, marked irregularity in shape and size of the glands, variations in the shape and size of epithelial cells, heaping up of the epithelium to several layers in thickness, loss of normal polarity of the cells, a relative decrease in amount of cytoplasm and an increase in size of nuclei, an absence or marked increase in secretory activity to such an extent that the cells may be partially or completely destroyed by, and the lumens of the glands distended with, secretion, irregularity, hyperchromatism and increased mitotic activity of the nuclei, and an infiltration of the stroma with leukocytic cells. In a small per

cent of cases, there is an associated metaplasia of epithelium to a stratified squamous variety and in some of these, an actual development of foci of squamous cell carcinoma (*adenoacanthoma*). Spread of the tumor occurs (1) by direct extension to the myometrium, cervix, parametrium, bladder and rectum, (2) by lymphatics to the iliac, hypogastric, aortic and inguinal nodes, (3) uncommonly, by the blood stream to the liver, lungs and other areas and (4) rarely, intraluminally to the fallopian tubes and ovaries.

The correct *diagnosis* is made from the history, examination of vaginal smear for neoplastic cells, and endometrial biopsy. *Treatment* consists of irradiation, hysterectomy or a combination of the two. Five year *cures* are reported as ranging from 40 to 60 per cent.



FIG 370.—Sarcoma of the uterus arising in a fibromyoma The tumor is soft, grey and friable.

Sarcoma of the uterus constitutes about 0.2 per cent of the more common uterine lesions and about 4 per cent of all malignant tumors of this organ. They are most common in the fifth decade of life. *Symptoms* may consist of metrorrhagia, menorrhage or post menopausal bleeding if the endometrial surface is affected or merely of a uterine mass if it is not. Sometimes metastasis to the lung or elsewhere first attracts attention. Pain, anemia, cachexia and weakness are late manifestations. Most frequently, the uterus is removed because of a "fibroid" and the correct diagnosis is not made until the specimen is examined in the laboratory.

Pathologically, the tumor may be found in the body or less often in the cervix. Its point of origin may be the stroma of the endome-

trium, muscle, connective tissue or blood vessels. In the literature, however, there is little or no attempt made to establish a histogenetic classification and the lesions are all lumped together under the heading "sarcoma." Grossly, two types may sometimes be recognized—one that starts as a sarcomatous degeneration of a fibromyoma and one that starts as a sarcoma. Frequently, however, the tumors when examined are so large that a distinction is not possible. As seen in the laboratory the growth often resembles a degenerated and necrotic fibroid (Fig 370). It is sharply circumscribed, moderately firm or soft, bulges on cut surface, is grey or greyish brown, may show areas of necrosis and hemorrhage, and measures as much as 20 cm in diameter. Histologically, the growths are extremely variable. Some of them resemble a cellular fibromyoma and have in fact been called "benign metastasizing fibromyomas." Usually

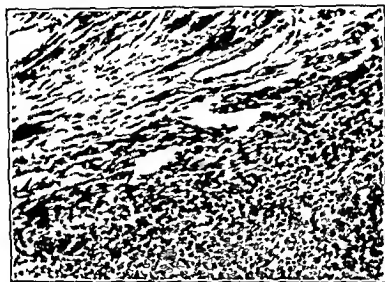


FIG 371.—Sarcoma of the uterus (same case as illustrated in figure 370) showing the line of transition from the fibromyoma to the sarcoma. $\times 100$

the cells are spindle or round, have a scanty or moderate amount of ill-defined cytoplasm, and disclose spindle, oval or round relatively large hyperchromatic nuclei (Fig 371). Bizarre tumor giant cells may be frequent and mitoses may be numerous. The degree of vascularity varies considerably. Spread is usually hematogenously to the lungs, liver, kidneys, peritoneum, bones and other tissues although lymphatic dissemination to draining nodes is also seen.

A clinical diagnosis of sarcoma as already noted is often difficult or impossible. A rapidly enlarging "fibromyoma" should arouse suspicion and in cases associated with vaginal bleeding, histologic examination of uterine scrapings is often diagnostic. Treatment is hysterectomy. The five year survival rate is less than 30 per cent.

Mixed tumors have also been called teratomas, botryoid tumors (because of a grape-like arrangement), and by various other names, such as rhabdomyosarcoma, chondrosarcoma, etc., depending upon the predominating tissue. They have been described as primary in

the vagina in infants and children, in the cervix at all ages and in the uterus usually beyond the age of forty-five years. The most constant *symptoms* are vaginal bleeding and discharge. Later there is considerable pain. *Grossly*, the growths in the vagina and cervix are arborescent, vesicular and resemble a hydatidiform mole. Those in the uterus are usually polypoid, flattened, fill and greatly distend the uterine cavity, and are attached by a sessile or narrow pedicle. *Histologically*, the most common neoplasms are composed basically of a mass of myxomatous or embryonal connective tissue with stellate cells, long protoplasmic processes and abundant watery matrix. If carefully examined, one will also find foci of striated and smooth muscle, hyaline cartilage, bone, osteoid tissue, fat, nerve tissue and epithelium. The latter is usually said to exist as inclusion foci but proliferations resembling carcinoma have also been described. *Spread* is, as a rule, locally to fill the entire pelvis and its containing organs. Rarely, metastases occur to the lungs, pleura, mediastinum and bones. *Treatment* has consisted of surgical removal and irradiation. The *prognosis* is poor. Most of the patients die within a year.

Mechanical Disturbances.—These may be considered briefly under four headings—changes in position, inversion, rupture and bleeding.

Changes in position of the uterus consist of: (1) *Retroversion*—backward tilting of the entire uterus but maintenance of its normal antelexion. (2) *Retroflexion*—when the body tilts backwards due to an increase in the anterior cervico-uterine angle. (3) *Prolapse*—This means a protrusion of the uterus into the vagina and is caused by injury to the fascial ligaments at the time of delivery. It may be partial or complete. In the latter the uterus presents itself at the vaginal orifice (procidentia).

Inversion of the uterus is an inside out transposition of the organ. While it may occur as a result of an extrusion of a submucous fibromyoma it usually follows the third stage of labor. In such cases, it may be spontaneous but more often it results from too much pressure upon the uterus or from pulling on the umbilical cord in an attempt to remove the placenta. Its incidence is reported as approximately one in 4000 deliveries; it is more common in primigravida, and it is accompanied by hemorrhage and shock. *Treatment* is immediate replacement. If the condition remains unrecognized it is followed by incarceration, strangulation, necrosis and local and systemic infection.

Rupture of the uterus is a tear that usually eventuates from an internal or external force or from muscular contraction of the organ. It may be complete in which case it extends from the uterine cavity through the serosa, or it may be incomplete when it stops short of the peritoneal covering. The latter is practically always associated with a hematoma. The condition is, as a rule, found in pregnancy. The predisposing factors consist of scar from a previous caesarean section, fibrosis of the cervix with thinning of the lower uterine segment, polyhydramnios, degenerating tumor in the wall of the uterus, hypoplasia of the uterus and pregnancy in rudimentary horn.

In addition, a normal myometrium may be ruptured by manual manipulation

Bleeding from the vagina is normal when it occurs rhythmically every twenty-five to thirty-five days between the menarche and the menopause. Abnormal bleeding at the time of menstruation is known as *menorrhagia*, abnormal bleeding between periods is called *metrorrhagia*, a combination of both is known as *menometrorrhagia*, absence of bleeding is referred to as *amenorrhea*, and painful menstruation is called *dysmenorrhea*. The causes of these disorders are many. Some are organic and demonstrable, while others are less apparent. The former are similar to those which account for postmenopausal bleeding and may be listed as follows: (1) Carcinoma or other tumors anywhere from the vagina to the ovaries. (2) Inflammations and ulcerations of the urethra, vagina, cervix, and uterine body and less frequently of the fallopian tubes. (3) Mechanical disturbances, such as foreign bodies in the vagina, direct trauma to the vagina, cervix or uterus proper, and prolapse of the uterus. (4) Systemic disorders such as blood dyscrasias and leukemias. In addition, bleeding during the child-bearing period may be caused by disturbances of pregnancy and may be listed as abortion, ectopic pregnancy, hydatidiform mole, placenta praevia, premature separation of the placenta and atony of the uterine musculature after delivery.

FALLOPIAN TUBES

ANATOMY

The fallopian or uterine tubes are two in number. Each is attached to the upper and lateral surface of the body of the uterus, extends laterally along the superior border of the broad ligament, and measures approximately 10 cm in length and 0.5 to 1.0 cm in diameter. Medially—laterally each tube consists of (1) a *uterine portion* that traverses the myometrium, (2) a narrow *isthmus* adjacent to the uterus and comprising about one-third of the entire length, (3) an *ampulla* that is broader and composes the middle third and (4) a *fimbriated end* or *infundibulum* adjacent to the ovary.

Histologically, there are three coats, (1) a *mucosa* that is thrown into numerous tall folds in the ampulla, smaller folds in the isthmus and mere ridges in the uterine portion. The epithelium is stratified pseudocolumnar and decreases in height from the fimbria to the uterus. It consists of two types of cells—ciliated and secretory. The lamina propria is composed of scanty connective tissue which contains scattered mononuclear cells, (2) a *muscle* coat consisting of an inner circular or spiral layer and an outer longitudinal layer, (3) a *serous* coat externally. Slight cyclic changes occur in the epithelium during the menstrual cycle. At or beyond the climacteric the connective tissue of the folds becomes hypertrophied and sclerotic and the folds become broader and lose their convolutions. The covering epithelium loses its cilia and the cells become flatter. These alterations are referred to as *sclerotic* or *senile changes*.

PATHOLOGY

Congenital Anomalies.—Developmental malformations of the fallopian tubes consist of the following: (1) *Occlusion*. This may involve the entire length or only a portion of a tube. It is one of the commonest causes of sterility. (2) *Double fimbriae*, one of which is usually rudimentary. (3) *Diverticula*. (4) *Rudimentary tube*, as a rule, in conjunction with non-union of the tubes or absence of the uterus. (5) *Absence*. This is rare, is usually seen in a one horned uterus and is often associated with absence of the ovary and kidney on the same side.

Inflammations.—An inflammatory lesion of a fallopian tube is known as *salpingitis*. It may be divided into (1) non-specific, which may be subdivided into acute and chronic, and (2) specific or granulomatous, which for practical purposes consists of tuberculosis, but which also includes *syphilis* and *actinomycosis*.

Acute Salpingitis.—This is caused by the gonococcus or other pyogenic organisms. The *gonococcal* form is said to account for more than one-half of all cases. The organisms reach the tubes by ascending along the lumen of the cervix and body of the uterus. In the tubes, the brunt of the attack is, therefore, borne by the mucosa. *Grossly*, the organ becomes swollen, red, moderately firm and rigid. At first the fimbriated end is patent and thick creamy pus drips freely into the pelvis and gravitates to the cul-de-sac. Soon, however, the fimbriae become plastered to each other, to the ovary and to adjacent structures. *Histologically*, the lumen contains neutrophils; the folds are broadened, congested, edematous and infiltrated with neutrophils and fewer plasma cells and lymphocytes, and the epithelium in patchy areas becomes degenerated and ulcerated. *Clinically*, there are pain, malaise, dysuria, leukorrhea, fever, painful defecation, anorexia, nausea and vomiting. If reinfection is wanting, many of the inflammations resolve completely or have only residual adhesions. Others, and particularly those with repeated infection, pass on to the subacute and chronic stages, to localized peritonitis, or to the formation of an acute pelvic or tubo-ovarian abscess.

The acute pyogenic form of the disease of *non-gonococcal origin* is caused by streptococci, staphylococci, proteus bacilli or colon bacilli. Such infections usually follow parturition or abortion and reach the fallopian tubes and parametrial tissue by lymphatic channels and blood vessels. Because of the primarily interstitial spread of the inflammation, the extra-luminal tissues become more congested, swollen and pus soaked than they do in gonococcal infection. Otherwise, the histologic changes are similar.

Chronic Salpingitis.—This usually represents repeated inflammatory insults to the fallopian tubes and is, therefore, often gonococcal in origin. The *gross* appearance varies considerably. At one extreme, there may be only moderate thickening and fibrosis of the wall with or without scattered adhesions. At the other extreme, not only the tubes but all the pelvic organs are matted together to form a solid, distorted mass of fibrous tissue and pus pockets wherein

none of the structures is identifiable. Between these two extremes, there are many gradations. In one type single or multiple nodules occur in the isthmus that have been called "*salpingitis isthmica nodosa*." They are composed of gland-like or re-epithelialized spaces within the wall that are set in a stroma of fibrous tissue. When pus collects between the fimbriated end and ovary, a *tubo-ovarian abscess* forms. An accumulation of pus within the tube is called a *pyosalpinx*. In long standing processes, the purulent material is resorbed, watery fluid remains and the condition is known as a *hydrosalpinx*. When the wall of such a tube is vascular and some of the vessels rupture with resulting hemorrhage into the tube, the lesion is referred to as *hematosalpinx* (some cases also caused by ectopic pregnancy) (Fig. 372). In all of these, there may or may not be a communication with the ovary. Usually the folds of the tube become adherent to



FIG. 372.—Hematosalpinx. There is a communication between the dilated tube and a cyst of the ovary.

each other to form gland-like spaces producing what has been called *follicular salpingitis*. Abscesses are not confined to the fallopian tube and ovary but are also found in the pelvis proper. In each of these locations the collection of purulent material may remain walled off and in time be resorbed. At any time, however, as a result of trauma or spontaneously, the wall may break and the infection may then spread to produce a local or general *peritonitis*, or the abscess may burrow into the intestine, bladder, cervix or vagina and produce a *fistula*.

Tuberculosis Salpingitis—This is said to constitute from 1 to 10 per cent of all infections of the fallopian tubes. It is almost always secondary to tuberculosis elsewhere in the body, although the primary focus may be difficult to find. Previous tubal inflammation and hypoplasia are thought to be predisposing factors. The disease occurs most frequently between the ages of twenty and forty years, less often in childhood and rarely after the menopause. *Symptoms*

may be acute and consist of pain and tenderness in the lower abdomen or they may be vague with only pelvic distress. There may also be menorrhagia, anemorrhœa, often sterility, dyspareunia, leukorrhœa and bouts of fever. *Grossly*, one or both tubes are enlarged, tortuous and studded with grey tiny or larger nodules. Cut surfaces may appear fibrous and disclose tubercles, or the entire central portion may be replaced with a cheesy, caseous mass. Calcium may be present. *Histologically*, the tubercle is the characteristic unit. While the disease may remain localized for long periods, the danger of systemic dissemination or of rupture and peritoneal spread is always present. *Treatment* is salpingectomy or irradiation. The *prognosis* is good if the active disease remains confined to the tubes.

Tumors.—Neoplasms of the fallopian tube and uterine ligaments are not frequent. They may be listed as follows: from epithelium, a carcinoma; from embryonic elements, hydatids of Morgagni (dilated blind ends of Gartner's ducts), and para-ovarian cysts (dilated Gartner's ducts covered with overstretched fallopian tube, thin walled, filled with clear fluid and lined with cuboidal or flattened cells); from connective tissue, a fibroma; from muscle tissue, a myoma; from muscle and fibrous tissue, a fibromyoma; from "mesodermal tissues," a sarcoma; from mesothelium, a mesothelioma; from chorionic elements, a chorionepithelioma; from reticulum cells, a plasmacytoma; from distant or adjacent areas, carcinoma (particularly of the endometrium or ovary), and endometriosis.

Carcinoma.—Carcinoma of the fallopian tube is reported as constituting from 0.16 to 0.45 per cent of all primary malignant tumors of the female genital tract. It occurs most frequently between the ages of forty-five and fifty-five years with extremes of eighteen and eighty years. *Symptoms* consist of bloody to watery vaginal discharge, pain in the lower abdomen on the side of involvement and, rarely, a lower abdominal swelling. Pelvic examination may reveal a mass that measures as much as 15 cm. in diameter. The right tube is affected as frequently as the left and the tumor is bilateral in 6 per cent of cases. *Grossly*, the lesion may be quite deceiving, for it may not only resemble but is often associated with pyosalpinx, hydrosalpinx and hematosalpinx. In other cases, the entire tube is filled and distended with a pinkish grey, soft, friable tumor. In the late stages, it has a tendency to penetrate the wall and involve the serosa. *Histologically*, it is composed of papillary or adenomatous structures or a mixture of the two. The cells are cuboidal or columnar, non-ciliated, and a single or double layer in thickness. The cytoplasm is moderate in amount and the nuclei are large, round, oval or irregular, hyperchromatic and disclose varied numbers of mitoses. In the more undifferentiated forms, the arrangement is less regular; the cells are more bizarre, and there is considerable necrosis. *Spread* takes place to the peritoneum with the production of ascites, to the inguinal, iliac and aortic lymph nodes, to the uterus fairly frequently but to the ovary rarely, and also infrequently to the lungs and liver. *Treatment* is total hysterectomy and bilateral salpingo-oophorectomy. The *prognosis* is poor.

Mechanical Disturbances—These may be considered under torsion and ectopic pregnancy

Torsion—This may affect the hydatids of Morgagni, paraovarian cysts or a fallopian tube. The latter may be normal (except for being attached by a long mesosalpinx) or it may be enlarged because of disease. The most common afflictions predisposing to torsion are hydrosalpinx, pyosalpinx, hematosalpinx, tumor and ectopic pregnancy. Exciting causes are muscular effort, contractions of the bladder and intestines, external pressure, disturbance of equilibrium of the tumor, and fall or jolt. Torsion may be recurrent, incomplete or complete and may result in gangrene or spontaneous amputation. It is accompanied by symptoms and signs that simulate appendicitis.

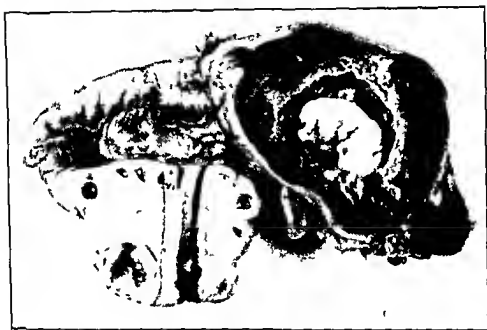


FIG. 373—Ectopic pregnancy showing the fetus in the dilated proximal end of the uterine tube

Ectopic Pregnancy—This disturbance may be defined as pregnancy occurring elsewhere than in the uterine cavity. Normally, the ovum is fertilized in the fimbriated end or the ampulla, sojourns through the tube in about three days, and implants in the endometrium on approximately the eighth day. Abnormal implantation occurs if its sojourn in the tube is delayed or if its descent is too rapid (in which case it may reach the cervix). The most common site of ectopic gestation is the fallopian tube. Other locations are abdominal cavity, ovary, broad ligament, abdominal wall and cervix. The causes of tubal pregnancy are (1) congenital stenosis and diverticula, (2) inflammation of any type with resulting adhesions, stenosis, diverticula, etc., (3) neoplasms within or without the tube, (4) mechanical disturbances as loss of ciliary action,

decrease or loss of peristalsis and occlusions resulting from plastic reconstructions and (5) physiological in the form of decidual preparation in the tubal mucosa. Tubal pregnancy accounts for about 1 per cent of all gestations, 3 per cent of gynecological operations and 1.5 per cent of gynecological admissions. The most common age is the third and fourth decades, and about one-third of the cases occur as the initial conception. *Clinically*, there are a history of amenorrhea for one or two periods, pain, vaginal bleeding or spotting, nausea and vomiting, shock, adnexal tenderness and mass, fullness in cul-de-sac, and a positive hormonal test for pregnancy.

Grossly, as seen in the laboratory the affected tube is usually fusiformly dilated to a diameter of 3 or 4 cm. The serosa is smooth, tense and intact, if rupture has not occurred, or it is irregularly lacerated, if rupture has previously taken place. Cut surfaces may reveal a placenta, membranes and an intact embryo, but more frequently these structures are not recognizable due to degeneration, necrosis and massive hemorrhage (Fig. 373). *Histologically*, there are chorionic villi, membranes, portions of an embryo and usually a decidua that is less well developed than that in uterine pregnancy. In addition, there are frequently inflammatory or other alterations in the tube. Changes in the *endometrium* consist of decidual reaction which may be extruded as a cast and secretory activity of the glands. While in most cases the fetus dies and is destroyed, in rare instances it develops to maturity. Death and petrification, however, may occur at any time to produce what is known as a *lithopedion*.

The *diagnosis* of ectopic pregnancy is made from a careful history, adnexal tenderness and mass, fullness of and blood in the cul-de-sac, endometrial biopsy and a positive Aschheim-Zondek test. *Treatment* is salpingectomy. The *mortality* should be less than 3 per cent.

OVARIES

ANATOMY

The *ovaries* are two in number, are located one on each side of the pelvis, are attached to the posterior surface of the broad ligament, and are situated below the fallopian tube. Each measures about 3 x 1.5 x 1 cm. and presents (1) a tubal extremity to which are attached a suspensory ligament and fimbria of the fallopian tube, (2) a uterine extremity also exhibiting a ligament, (3) lateral surface (4) medial surface, (5) free border directed towards the ureter and (6) mesovarian border which is attached to the back of the broad ligament and through which pass the vessels and nerves. The *arteries* are the ovarian arteries; the *veins* form a pampiniform plexus that drains into ovarian veins which accompany the arteries; the *lymphatics* drain into the lateral and pre-aortic nodes, and the *nerves* are derived from the hypogastric or pelvic plexus, the ovarian plexus and uterine nerves.

Histologically, the ovary discloses an outer single layer of *germinal epithelium*, an underlying layer of connective tissue called *tunica albuginea*, an inner stroma of reticular fibers and spindle cells

(special connective tissue) and *follicles*. In the new born, the latter number about 400,000 (both ovaries). Subsequently, they decrease in number mostly as result of atresia but some as a result of ripening and ovulation. *Primary follicles* measure about 45 microns in diameter. They consist of a central ovum and peripheral follicular cells, and develop into *Graafian follicles* by division of the latter and accumulation of follicular fluid. The surrounding stroma forms a capsule of *theca cells*. In the mature follicle which measures about 5 mm. in diameter, the follicular cells form the granulosa membrane and the theca cells are recognized as an internal layer of larger polyhedral lipid containing cells and an external layer of more compact and primitive cells. Rapid accumulation of fluid finally eventuates in rupture of the follicle, after which the follicular epithelium and theca internal cells become the large pale staining cells of the *corpus luteum*. The cavity of the latter is filled with follicular fluid, serum and a few erythrocytes. If the ovum becomes fertilized the corpus luteum enlarges to become one of pregnancy, otherwise it rapidly degenerates, becomes fibrotic and is transformed into a *corpus albicans*.

PATHOLOGY

Congenital Anomalies—Developmental malformations of the ovary may be listed as follows: (1) *absence* of one or both ovaries, frequently associated with other genital malformations, (2) *failure of descent*, (3) *accessory*, (4) *hypoplasia*, usually associated with poorly developed primary and secondary sex characteristics, (5) inclusion of aberrant *adrenal tissue* and (6) *ovotestis*, that is, inclusion of testicular tissue. This is found in connection with true hermaphroditism.

Inflammations—Inflammation of an ovary is called *oophoritis*. Most of the lesions by far are associated with inflammation of the fallopian tubes and adjacent tissues and are, therefore, contracted by direct extension or by lymphatic metastasis. The causative organisms are similar to those producing salpingitis. As in the latter, the infection may be *acute* or *chronic* and the ovaries may be large, edematous, soft and succulent, or they may be firm, fibrous covered with adhesions and part of a tubo-ovarian abscess. Histologic changes are those of acute or chronic non-specific inflammation. Granulomatous lesions of the ovary are much rarer. There have been described *tuberculosis*, *gumma*, and *actinomycosis*.

Tumors—Classifications of neoplasms of the ovaries are, as a rule, varied, lengthy and confusing. The chief reason for this is the fact that there are many more tumors than there are tissues to account for them. Speculation, therefore, regarding the origin of some of the tumors is not lacking and because of this, contrary to tumors of other organs, a histogenetic classification seems inadvisable. The more common growths may be listed as follows: (1) simple cysts—follicle, theca luteum, corpus luteum, endometriosis, germinal inclusion, (2) serous cystadenoma, (3) pseudomucinous cystadenoma, (4) dermoid cyst, (5) fibroma, (6) carcinoma, (7) mesonephroma, (8) chorionepithelioma, (9) secondary tumors, (10) granulosa cell

tumor, (11) theca cell tumor, (12) arrhenoblastoma, (13) adrenal adenoma, (14) Brenner's tumor and (15) dysgerminoma.

Obviously, in the space available, only a cursory account of each growth is possible. For more detailed descriptions and for numerous references to the more recent literature, the reader is referred to the excellent reviews by Dockerty and Block. Also to save space and repetition, the *clinical manifestations* of the non-endocrine tumors might be dispensed with here. Unless accompanied by torsion of the pedicle or rupture, most tumors of the ovaries are symptom free until they become quite large. The most common complaint is swelling of the abdomen. This develops slowly if the tumor is benign, and rapidly if it is malignant. It is due to the growth as such or to the accompanying ascites or both. The ascites may be caused by partial venous obstruction within the tumor or by peritoneal irritation from cancerous implants. Other manifestations are (1) pain due to volvulus, rupture, adhesions, infection and pressure upon adjacent structures, (2) gastro-intestinal disturbances such as nausea, vomiting, indigestion and constipation, (3) urinary alterations, (4) symptoms from distant metastases and (5) a demonstrable, pelvic, adnexal or abdominal mass. *Treatment* of all ovarian tumors is surgical excision. If the lesion is benign a local extirpation is all that is necessary, but if it is malignant and operable both ovaries, fallopian tubes and entire uterus should be removed. As an added precaution, some clinicians follow this by irradiation therapy. Others, however, do not subscribe to this procedure. The *prognosis*, as would be expected, varies. In general, the more differentiated the tumor the better is the outlook, but it must never be forgotten that seemingly completely extirpated tumors of low grade malignancy may recur ten, fifteen or more years postoperatively.

Follicle cysts are common. They represent follicles that have failed to rupture, usually measure from 0.5 to 5 cm. in diameter, are often multiple and bilateral, have smooth surfaces, and are filled with clear fluid, although hemorrhage from ruptured mural capillaries is common. Histologically, the lining is composed of regular or attenuated granulosa cells. Sometimes, however, all these cells disappear and the lining is composed of fibrous tissue or luteinized theca cells. The latter are, therefore, called *theca lutein cysts*. They are commonly associated with hydatidiform mole and chorion-epithelioma.

Corpus luteum cysts measure from 2 to 6 cm. in diameter, are filled with bloody or brown fluid, and disclose an inner lining of light yellow or orange yellow tissue. Histologically, recent cysts are lined with well preserved lutein cells whereas older cysts show degeneration of these cells and an increase of peripheral fibrous tissue.

Endometriosis has already been considered in connection with the uterus. It should be emphasized here that all bloody or chocolate-like cysts of the ovary are not endometrial and that in fact corpus luteum cysts and hemorrhagic follicle cysts are much more common.

Germinal inclusion cysts are common, but as such are of no clinical significance. They are often microscopic in size, found just

beneath the germinal epithelium and are lined with cells similar to those covering the surface of the ovary

Serous cystadenomas occur most frequently between the ages of twenty and fifty years and are not found before puberty. Their origin, not agreed upon, is said to be from germinal epithelium, from tubal rests, from Wolffian remnants and from teratomas. They are bilateral in about 30 per cent of the cases and measure from 3 to 15 cm. in diameter, although they may at times fill the entire abdomen.

Grossly, the external surface is usually smooth but in some cases it is covered with papillary excrescences. The wall is thin and fibrous. Cut surface discloses a single or a multiloculated cavity with a smooth or papillary covered lining (Fig. 374). The papillae

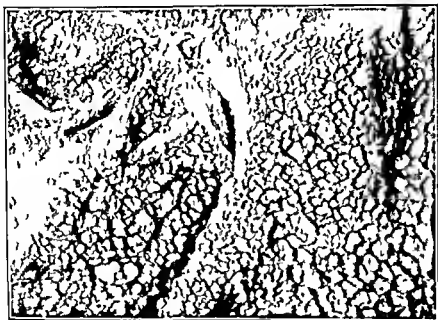


FIG. 374.—Papillary serous cystadenoma of the ovary.

may be few in number and difficult to find or they may be so exuberant as to fill most or all of the cyst. The contents consist of serum-like fluid, but when hemorrhage has occurred it may be of a brown color. *Histologically*, the lining epithelium consists of a single layer of cuboidal or flattened cells that in some areas resembles germinal epithelium and in others tubal epithelium. The latter is composed essentially of ciliated cells, interspersed with which are taller, non-ciliated, peg or pear-shaped cells with scanty cytoplasm. Frequently, the epithelium is denuded. The papillae are covered with similar epithelium. Their cores are composed of thin or club shaped masses of loose, myxomatous or dense fibrous tissue. Scattered through the wall and between the papillae, there are often present small laminated, bluish stained, calcific deposits called psammoma bodies.

Papillary serous cystadenoma have a tendency to become *malignant*. While in bona fide cases such a transformation may be easy to detect, there are cases in which the change is more subtle. In such instances, the following alterations are significant: stratification of the epithelium to one of several layers in thickness, loss of polarity of the cells, a relative increase in nuclear material, hyperchromatism, increased mitoses, irregularity in shape and size of the cells, and invasion of the fibrous tissue wall.

Pseudomucinous cystadenomas are so-called because their contents consist of a mucin-like fluid which differs from mucin. Their origin is uncertain and is relegated to Mullerian inclusions, Wolffian remnants and teratomas. They constitute about one-

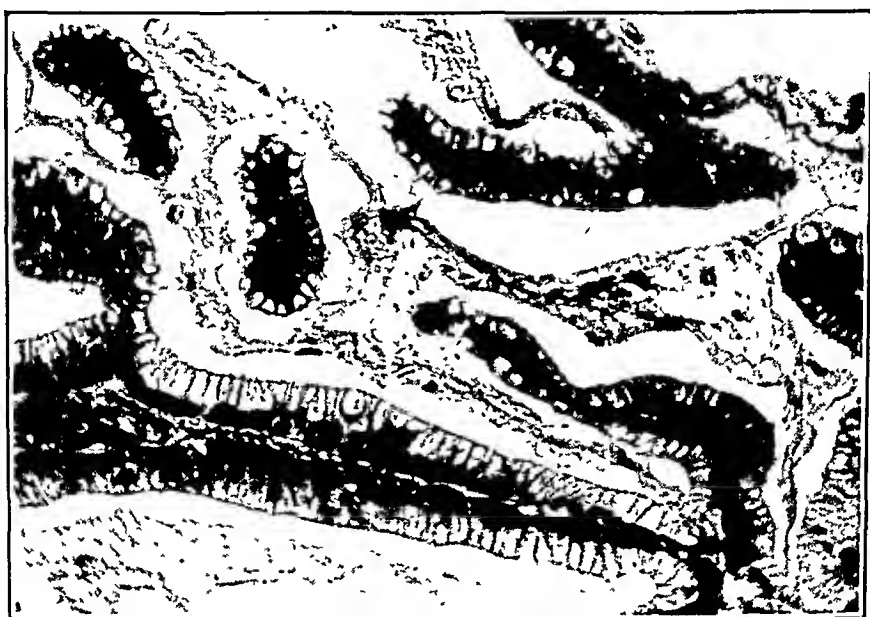


FIG 375 —Pseudomucinous cystadenoma of the ovary showing tall columnar cells with basilar nuclei and secretion in their cytoplasm x 100.

quarter of all ovarian neoplasms and occur during the reproductive period of life.

Grossly, the tumor is unilateral in four-fifths of the cases and frequently grows to large proportions often filling most of the abdomen. Externally it is smooth, lobulated, pedunculated and may or may not be adherent to adjacent structures. The wall is thin, fibrous and often bluish in color. Cut surfaces disclose numerous small and large cavities filled with a grey, straw colored or brown thick or thin fluid. Unlike serous cysts the inner surface discloses papillae in only about 6 per cent of cases. *Histologically*, the lining is quite characteristic. It consists of a single layer of tall, slender, columnar epithelium orderly arranged upon a distinct basement membrane (Fig. 375). The nuclei are oval or elongated, deeply stained and basilar. The supranuclear cytoplasm is distended with secretion which, with rupture of the cell borders, is seen to stream into the lumen of the cysts. Alterations in this typical epithelium occur as a result of pressure and more rapid growth. In

the former, it may be flattened or entirely destroyed. In the latter, it tends to be lower, to show less secretion and to be more deeply stained. The capsule and septa are fibrous and are usually invaded by the regular cells whereby new cysts are produced.

Pseudomucinous cystadenomas become *malignant* in only about 5 per cent of the cases. In such instances, the tumor becomes adenomatous, the lining cells are cuboidal and several layers thick, and they reveal the irregularities usually seen in carcinoma. Another complication in some of the cysts that rupture intraperitoneally is *pseudomyxoma* of the peritoneum. This is discussed in Chapter XIV.

Dermoid cysts of the ovaries are better considered as teratoid tumors, for if a diligent search is made elements representing the three germinal layers are usually found. The histogenesis of these tumors is not settled. They are considered to arise from cell rests, from misplaced blastomeres and from unfertilized ova. They constitute about 10 per cent of all ovarian tumors, are rare in infants and children and are most common during the reproductive period of life. Roentgenograms are often diagnostic in that they show a radiolucent central area, bone, teeth, etc.

Grossly, the tumors are bilateral in about 15 per cent of the cases. They vary in size from 2 to 20 cm., are round or ovoid, smooth and cystic while in the body, but more solid and doughy after extirpated due to congealing of the contents. On section they are usually composed of a cyst that is filled with greasy sebaceous material mixed with hair. Protruding from the wall, there is, as a rule, a hillock to which are attached hair, teeth, cartilage, bone, etc. Within the lumen or within the wall, other organoid structures may be identifiable. A minority of the tumors are solid and even more complex. *Histologically*, the cyst is usually lined with respiratory and stratified squamous epithelium. The wall contains hair follicles, sebaceous and sweat glands, cartilage, bone, intestinal epithelium, connective tissue, muscle, brain tissue, thyroid gland, etc. In more solid growths one of these tissues frequently becomes malignant and outstrips the others, sometimes to such a degree that the tumor appears to be homogeneous.

Struma ovarii, as the term indicates, means a thyroid tumor of the ovary. It doubtlessly represents a one-sided development of an ovarian dermoid cyst, for remnants of the latter are almost always encountered if the specimen is examined carefully. The tumor usually exists as an adenoma, may be functionally active, histologically appears as thyroid tissue from the gland proper, and occasionally becomes malignant.

Fibromas of the ovary are found at all ages after the menarche. They grow slowly and, aside from twisting of the pedicle, produce symptoms by enlargement of the abdomen. This is due to the tumor itself, but in 40 per cent of cases it is the result of an accompanying ascite. The origin of the peritoneal fluid is venous obstruction within the tumor, due probably to partial rotation of the pedicle. From the abdominal cavity, absorption occurs through the diaphragmatic lymphatics and fluid accumulates in the thoracic

cavities to produce what is called *Meig's syndrome*. It might be added here that these events also occur in connection with other ovarian tumors and are not specific for fibromas.

Grossly, the neoplasm is unilateral in 90 per cent of the cases. Its average size is about 8 cm. in diameter, but some measure over 20 cm. across. The external surface is smooth and often somewhat bossed. The consistency is firm. Cut surfaces are solid greyish white, but sometimes focal degenerations result in small cysts. The color changes to red or brown in the presence of infarction. Occasionally, calcific deposits are found. *Histologically*, some are composed of semi-whorled collections of spindle cells with wavy nuclei that resemble normal ovarian stroma. Others reveal masses



FIG. 376 —Carcinoma of an ovary A thin capsule encloses many large masses of solid tumor.

of cells that are more plump and resemble sarcoma. Hyalinization, edema, calcification and microscopic cyst formation are also encountered. Fibromas can be distinguished from theca cell tumors only by the absence of cytoplasmic fat granules.

Carcinoma of the ovary is the most serious neoplasm of this organ. Some of the cancers obviously arise in originally benign tumors such as cystadenoma, dermoid, granulosa cell tumor, dysgerminoma and arrhenoblastoma, but others are doubtlessly malignant from the start. The origin of the latter is not agreed upon. Among others, the tissues listed are salpingeal inclusions, germinal epithelium, Mullerian rests, adrenal rests, Wolffian remains and endometrial tissue. Cancer of the ovaries occurs at all ages but more than 50 per cent are found after the menopause.

Grossly, the tumors are found bilaterally in almost one-half of the cases. Some of the benign neoplasms that become malignant show no gross alteration. Others, and particularly the cystic tumors, reveal solid areas of rather soft brain-like tissue that discloses foci of necrosis and hemorrhage. Others still disclose penetration of the capsule, adherence to adjacent structures and peritoneal dissemination. Growths that are malignant from the start are solid or cystic. The latter are frequently indistinguishable from benign cystic tumors that have become cancerous (Fig 376). Solid carcinomas vary in size from a few to 20 cm or more. Externally, they are round, bossed, smooth or granular and papillary. They are soft to hard and on section present a variegated surface of white, grey, yellow, brown or red tissue that is traversed by fibrous septa. Foci of necrosis, hemorrhage and liquefaction are common. *Histo-*



FIG 377—Poorly differentiated papillary adenocarcinoma of the ovary x 100

logic patterns are quite variable. The most common is an adenomatous and papillary structure (Fig 377). These resemble the papillary cystadenoma. They are composed of large and small acini, some with and others without papillary infoldings or primarily of long arborizing papillae which by adherence produce a glandular structure. The lining cells are usually two or more layers thick and are cuboidal polygonal or irregularly shaped and of varying sizes. Their cytoplasm varies in amount but is usually moderate and it may be solid or vacuolated. The nuclei are round, oval or bizarre, hyperchromatic and disclose a few or many mitoses. The stroma is dense and fibrous. It is scanty in some cases but dominates the picture in others. Aside from this more common variety, there are tumors that on the one hand are composed of solid sheets and masses or irregular epithelial cells with practically no stroma and with frequently extensive necrosis. On the other hand, there are tumors composed of only few nests or cords of solid or glandular

cells and a fibrous stroma that dominates the picture. In general, microscopically as grossly, the neoplasms that arise in previously benign tumors have a tendency to reproduce the parent growth.

Spread of carcinoma of the ovary, occurs by (1) extension to the tube, uterus, intestines and bladder, (2) drop metastasis to the peritoneal cavity with the production of hemorrhagic or serous ascites, (3) lymphatic permeation to the lumbar, para-aortic and inguinal nodes and (4) hematogenous metastasis to the liver, lungs, bones and other organs and tissues. The former two are by far the most frequent.

Mesonephroma is a term used to designate certain usually cancerous growths that supposedly arise in mesonephric tissue. Grossly, they resemble solid or cystic carcinomas. Histologically, they tend to produce tubular structures that often disclose tufts,

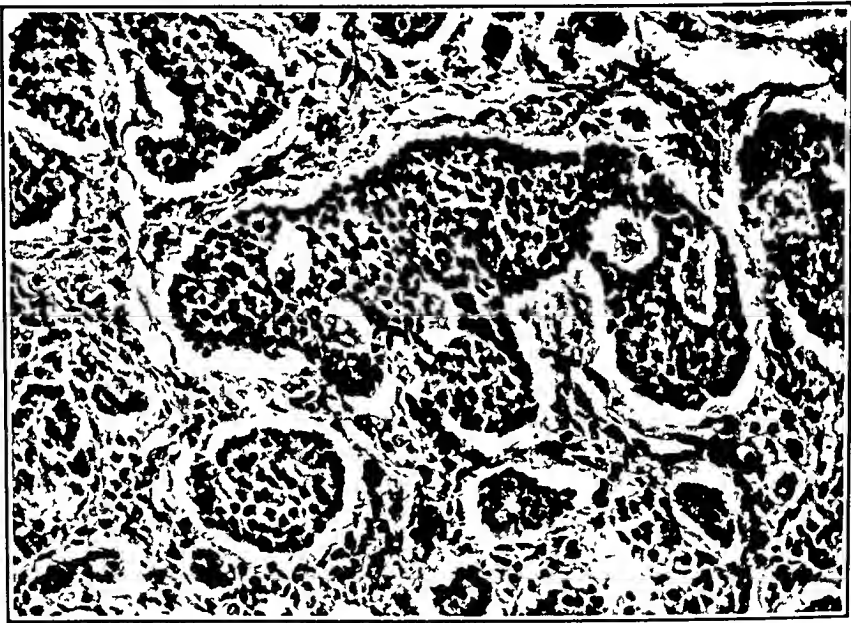


FIG 378 —Granulosa cell tumor showing nests of uniform appearing deeply staining cells set in a scanty fibrous tissue stroma. x 100

thus simulating renal glomeruli. Many authors are reluctant to accept this as a separate group of neoplasms.

Chorionepithelioma is rare in the ovary. It occurs as a metastatic lesion from the uterus, as primary in ectopic pregnancy of the tube and ovary, and uncommonly as a one-sided development in a teratoma. The lesion is described further in the section on the placenta.

Secondary tumors of the ovaries are common. They are usually bilateral, arise most frequently in the gastro-intestinal tract (particularly the stomach) and are then known as *Krukenberg tumor*. The primary focus may be so small that it is easily overlooked and it, therefore, behooves the operator to examine the intestinal tract in any tumor that involves both ovaries. Grossly, the ovaries are small or large and solid or cystic. Histologically, the epithelium is usually scanty in amount and exists as "signet ring" cells. It may, however, form adenomatous structures. The route of involve-

ment is by drop metastasis, lymphatic or blood vessel dissemination, or direct extension. Aside from intestinal cancers, tumors from any other organ, and particularly the breast, may secondarily affect the ovaries.

Granulosa cell tumors are feminizing (estrogenic) tumors that arise from mesenchyme. If they occur before the age of puberty they cause precocity, if during the reproductive period they result in initial amenorrhea followed by irregular periods, and if after the menopause they are accompanied by uterine bleeding that may simulate menstruation. Grossly, the tumors are several to 40 cm in diameter, usually solid and rarely cystic, and of a diffuse grey, brown or yellow color. Histologically, they are composed of small round or polyhedral cells with only a moderate amount of eosinophilic cytoplasm and round or oval deeply but uniformly stained nuclei (Fig 378). They tend to form follicles, cylinders, glands or large sheets of cells with varying amounts of stroma. In two-thirds of the cases, the endometrium is hyperplastic and in a greater than usual number in a comparative age group, it is neoplastic. Granulosa cell tumors are reported as cancerous in from 5 to 28 per cent of cases.

Theca cell tumors like granulosa cell tumors produce estrogens and are therefore feminizing. Grossly and histologically, they resemble fibromas and are distinguishable only by the presence of fat droplets in their cytoplasm.

Arrhenoblastoma is a rare masculinizing tumor that produces hirsutism, husky voice, hypertrophy of the clitoris, and amenorrhea. Its origin is uncertain. Grossly, the tumor is usually not more than 3 to 4 cm in diameter. Histologically, it may reproduce a testicle either partly or wholly, or it may present a diffuse sarcomatous appearance.

Adrenal adenoma of the ovary has among others been called masculinoblastoma. Its histogenesis is in dispute. It is extremely rare and in addition to the masculinizing symptoms found in arrhenoblastoma, there are hypertension, polycythemia and a tendency to diabetes and obesity. Grossly, the tumor is usually 2 to 3 cm in diameter and both macroscopically and histologically, it resembles adrenal cortical tissue.

Brenner's tumor probably arises in Walthard's nests (solid or cystic collection of epithelial cells found in the cortex of the ovary, the tubes and the uterine ligaments). They have no known endocrine function. They are few to 30 cm in diameter, usually solid and fibrous-like and may be found in the wall of a pseudomucinous cystadenoma. Histologically, the stroma is dense fibrous and abundant. It contains sharply circumscribed nests of solid epithelial cells with sharply or ill-defined borders, moderate cytoplasm and oval nuclei that resemble puffed wheat (Fig 379). Frequently, there is a small vacuole or cystic space in the center of the epithelial collection.

Dysgerminoma is said to arise in neutral or dysgerminal cells that are similar to the cells found in primitive gonads. It produces no endocrine disturbance and is usually found in pseudohermaphroditis.

or girls with poorly developed external genitals. The tumor varies in size from a few centimeters to one that fills most of the abdomen. It is well-encapsulated, moderately firm and on section presents a homogeneously grey surface with discolored yellowish areas. Histologically, it resembles seminoma of the testicle.

Mechanical Disturbances.—Under this heading may be briefly mentioned *torsion* of an *ovarian tumor*. The growth may be of any type and the most common age is the second to the fourth decades. The exact *cause* of the volvulus is not known but it is thought that venous congestion and the expansile force of the growth play a part. These are aided by the smooth surface of the tumor, a long pedicle, changes in intra-abdominal pressure and trauma. *Symptoms* and *signs* consist of pain, nausea and vomiting and abdominal tenderness.

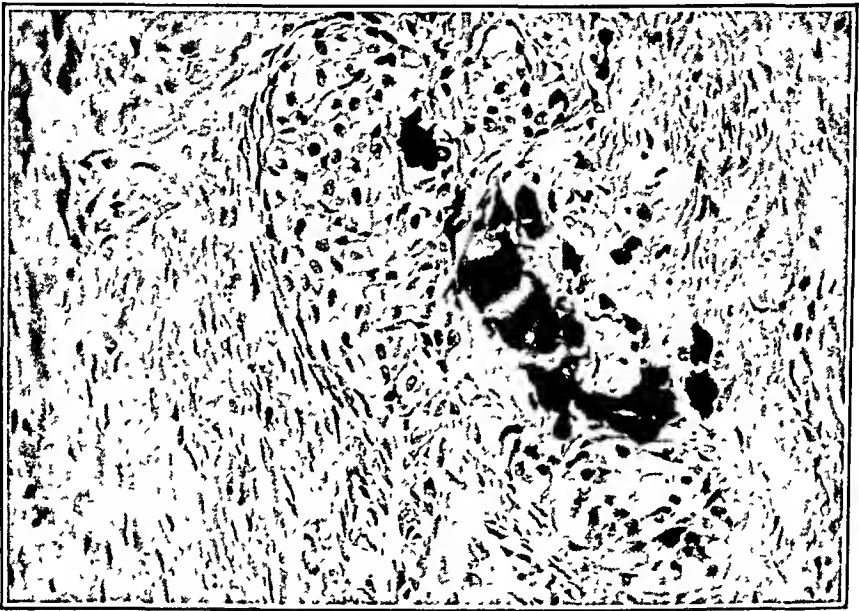


FIG. 379 —Brenner's tumor of the ovary. The stroma is dense and fibrous and contains foci of calcification. The tumor cells are sharply defined and contain folded nuclei x 100.

Pathologically, the turn in the right ovary is anti-clockwise and that in the left is clockwise. The tightness of the twist is more important than the number of turns. The venous return is blocked first, resulting in congestion and then hemorrhage into the lumen if the tumor is cystic. With increased pressure, the cyst may *rupture* and, rarely, it becomes infected. Occlusion of the arterial supply ultimately eventuates in necrosis and gangrene of the growth. *Treatment* is surgical extirpation.

PLACENTA

EMBRYOLOGY AND HISTOLOGY

Chorionic villi arise as projections from the surface of the blastocyst in the form of trophoblastic buds. The covering cells then differentiate into two layers—an inner of cuboidal cells called

Langhans' layer and an outer of ill-defined flatter cells with deeply stained oval nuclei called the *syncytial layer*. It is these trophoblastic cells that burrow into the endometrium which has been previously prepared and are responsible for the implantation of the placenta. When first developed the villi are large and contain a core of myxomatous connective tissue in which there are scarce extremely thin-walled capillaries. With the onset of the fetal circulation, which occurs about the fifth week of embryonic life, the vascularity gradually increases to keep pace with nutritional demands. About mid-way through pregnancy the Langhans' cells disappear entirely and the syncytial cells form polypoid masses of piled up nuclear material that resemble giant cells. With further aging, the villi become smaller and much more numerous. Their cores become more solid and gradually acquire many well formed moderately thick-walled capillaries.

ANATOMY

The mature placenta is a discoid mass that weighs about 500 gm and measures 15 to 20 cm in diameter and 3 cm in greatest thickness. The uterine or raw surface is divided by clefts into lobules that are called *cotyledons*. The opposite or fetal surface is smooth and intimately covered with amnion. The umbilical cord is inserted into this surface centrally or slightly eccentrically and from the point of attachment large sinuous veins and smaller arteries radiate peripherally.

PATHOLOGY

Congenital Anomalies—Developmental malformations of the placenta may be listed as follows: (1) Those associated with *twin pregnancies*, where there may be two placentas, two membranes and one placenta, and one chorion, two amnions and one placenta. (2) *Lobulations*—separation into one or more lobes by deep clefts. (3) *Succenturiate lobe*—separation of a portion that is attached to the main mass by membranes in which run vessels. A tear at this point may result in serious hemorrhage or retention of the accessory lobe within the uterus. (4) *Circumvallate placenta*—a folding of the membranes upon themselves about the periphery because of their separation from the chorionic plate by decidua. (5) *Velamentous insertion of the cord*, that is, where the cord is attached to membranes peripherally rather than over the placenta proper.

Inflammations—Inflammatory lesions of the placenta are not frequent. Ordinary *pyogenic* infection does not occur unless associated with abortion. The organisms ascend from below. The villi become degenerated, necrotic and remain as "ghosts" or they become disintegrated. There is a diffuse infiltration with neutrophils. *Tuberculosis* is extremely rare. The baby may or may not be infected. *Syphilis*, although frequently seen in parturient patients, does not reveal any pathognomonic changes. Compatible with luetic infection are enlargement and crowding of the villi, increase of cellularity and connective tissue of the cores, and a decrease

or girls with poorly developed external genitals. The tumor varies in size from a few centimeters to one that fills most of the abdomen. It is well-encapsulated, moderately firm and on section presents a homogeneously grey surface with discolored yellowish areas. Histologically, it resembles seminoma of the testicle.

Mechanical Disturbances.—Under this heading may be briefly mentioned *torsion* of an *ovarian tumor*. The growth may be of any type and the most common age is the second to the fourth decades. The exact *cause* of the volvulus is not known but it is thought that venous congestion and the expansile force of the growth play a part. These are aided by the smooth surface of the tumor, a long pedicle, changes in intra-abdominal pressure and trauma. *Symptoms* and *signs* consist of pain, nausea and vomiting and abdominal tenderness.

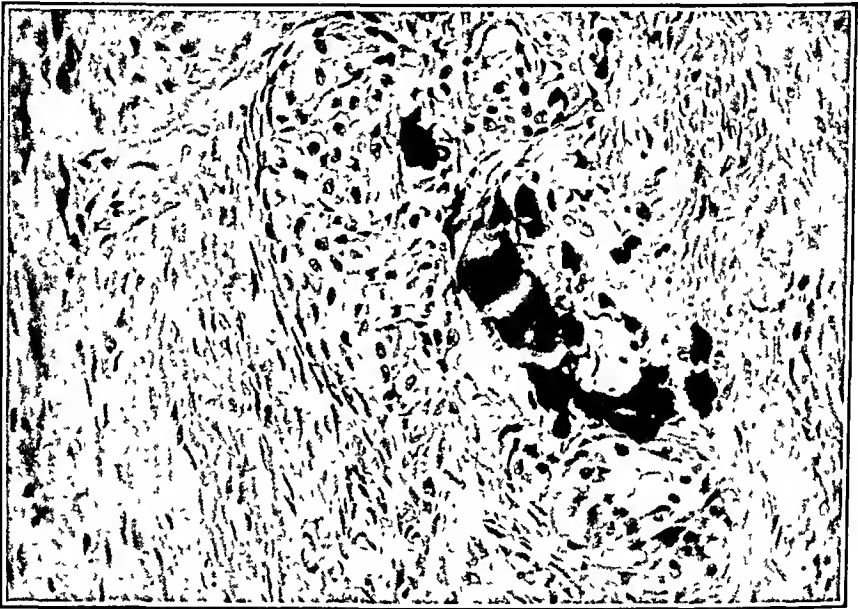


FIG. 379 —Brenner's tumor of the ovary. The stroma is dense and fibrous and contains foci of calcification. The tumor cells are sharply defined and contain folded nuclei x 100.

Pathologically, the turn in the right ovary is anti-clockwise and that in the left is clockwise. The tightness of the twist is more important than the number of turns. The venous return is blocked first, resulting in congestion and then hemorrhage into the lumen if the tumor is cystic. With increased pressure, the cyst may *rupture* and, rarely, it becomes infected. Occlusion of the arterial supply ultimately eventuates in necrosis and gangrene of the growth. *Treatment* is surgical extirpation.

PLACENTA

EMBRYOLOGY AND HISTOLOGY

Chorionic villi arise as projections from the surface of the blastocyst in the form of trophoblastic buds. The covering cells then differentiate into two layers—an inner of cuboidal cells called

of the myxomatous connective tissue composing the core and formation of large and small cystic masses that resemble clusters of grapes (Fig 380A). *Histologically*, the periphery is covered by hypertrophied, thickened, vacuolated, deeply stained syncytial masses that represent both the early fetal appearance and a true proliferation (Fig 380B). Beneath these, there is an overgrowth of cuboidal or polygonal sharply demarcated Langhans' cells with round or oval deeply stained centrally placed nuclei. The cores are composed of edematous or cystic myxomatous connective tissue that is poor in vessels and that frequently contains a granular precipitate. The ovaries often reveal corpus luteum cysts.

Hydatidiform moles occur at any time during the child bearing age, with an average around thirty years. The commonest *symptoms* are rapid enlargement of the uterus and uterine bleeding. The Aschheim-Zondek test is positive and the urine and blood show increased amounts of gonadotrophic hormone while viable chorionic tissue remains in the body. The *diagnosis* is made from the history, positive hormonal tests and examination of the mole passed by way of the vagina or obtained by curettage. *Treatment* is evacuation of the uterus. The *prognosis* is guarded temporarily, for about 5 per cent of the cases develop chorionepithelioma.

Chorionepithelioma—This is an extremely malignant but fortunately rare tumor. It is reported as constituting about 0.5 per cent of all malignant neoplasms of the female genital tract. It is more common in multipara and occurs at all ages during the reproductive period of life. Rarely, it arises beyond the menopause and then probably in a teratoma of the ovary. Its cause is not known but predisposing conditions are hydatidiform moles in 50 per cent of the cases and abortions, term pregnancies and ectopic pregnancies in the rest. The heralding *symptom* is uterine bleeding. It occurs several weeks to months after pregnancy, increases in severity and may be severe. Nausea and vomiting, pain and symptoms referable to distant organs (due to metastasis) follow. The Aschheim-Zondek test is positive and gonadotropins in urine and blood are elevated.

Grossly, the most characteristic features of a chorionepithelioma are its invasive properties and its tendency to degeneration, necrosis and hemorrhage (Fig 381A). The uterus is usually soft and bossed over the area of the tumor or diffusely enlarged. Cut surfaces disclose the neoplasm partly projecting into the endometrial cavity and partly penetrating the wall to varying depths. Sometimes, however, it is almost entirely intra-mural in which case a uterine curettage might prove unsuccessful. The lesion is usually ill-defined, has no semblance of a capsule, and is soft in consistency. The local growth is ordinarily not more than 6 to 8 cm in diameter. *Histologically*, it is composed of varying proportions of bizarre Langhans' and syncytial cells without villous formation. Langhans' cells as in normal villi are more orderly. They may appear in sheets, columns or singly and may be separate or partially covered by syncytial cells. They are often large, polygonal and have hyperchromatic nuclei. Syncytial cells also appear in columns or clumps

of their vascularity. Although not inflammatory, an *erythroblastotic placenta* may be considered here. If the disorder is severe enough to cause death of the child the placenta is increased in size and weight; the cotyledons are large, thick and sharply demarcated; the villi are enlarged and edematous; Langhans' cells are more numerous and the vessels contain immature erythrocytes and thrombi.

Tumors.—Under this heading may be listed a hemangioma, placental polyp (retained, attached and degenerated portion of pla-



FIG. 380 —Hydatidiform mole (A) Gross appearance composed of clusters of cysts and (B) histologic appearance showing a myxomatous connective tissue core covered by greatly proliferated syncytial masses. x 50.

centa), hydatidiform mole and chorionepithelioma. The latter two alone will be considered further.

Hydatidiform Mole.—This tumor is reported as occurring once in 240 to 20,000 deliveries depending upon the criteria used for its diagnosis. It may be defined as a partly degenerative and partly neoplastic myxomatous and cystic disorder of the chorionic villi. In its typical form, a mole can *develop* only when the ovum is deformed from the beginning and dies early. Because the ovum is dead the vascularity of the villi does not develop normally and the vessels which are already present tend to disappear. The trophoblastic epithelium, however, is viable and continues to function. Its secretions as usual pass into the villi and there accumulate for there is no fetal circulation to remove them. The result is separation

Mechanical Disturbances—These consist of (1) *placenta praevia*—implantation of the placenta in the lower uterine segment along the margin of or covering the internal os, (2) *infarction*—as in other organs, meaning stuffing with blood and causing death of the villi. In the placenta, vascular occlusion is due to subintimal accumulation of lipoid material. If recent, the area is sharply demarcated, enlarged and dark purple or black. With age, the affected portion shrinks and becomes grey or white and firm. Histologically, the former shows erythrocytic extravasation, while the latter discloses disappearance and fibrosis of the villi. Foci of *calcification* are common in infarcted placentas, (3) *placenta accreta*—abnormal adherence of the placenta to the uterine wall. It is due primarily to an absent or poorly developed basal decidua. Because of this, trophoblastic cells penetrate between the muscle fibers and steadfastly anchor the cotyledons to the myometrium, and (4) *knots* or *torsions* of the umbilical cord cutting off the fetal circulation and causing death of the baby.

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They are usually more irregular and vary from small somewhat spindle-shaped cells with confluent cytoplasm and intensely hyperchromatic nuclei to huge sharply or ill-defined tumor giant cells with piled up, irregular, deeply stained nuclear masses (Fig. 381B). The stroma is usually only moderate in amount or scanty. It is well vascularized and the tumor cells characteristically invade their lumens. Degeneration, necrosis and hemorrhage are common. *Spread* of chorionepithelioma is by direct extension through the myometrium into the broad ligaments, occasionally by lymphatics to the nodes, but most commonly by blood vessels to the lungs, vagina, brain, liver, ovary and other sites.

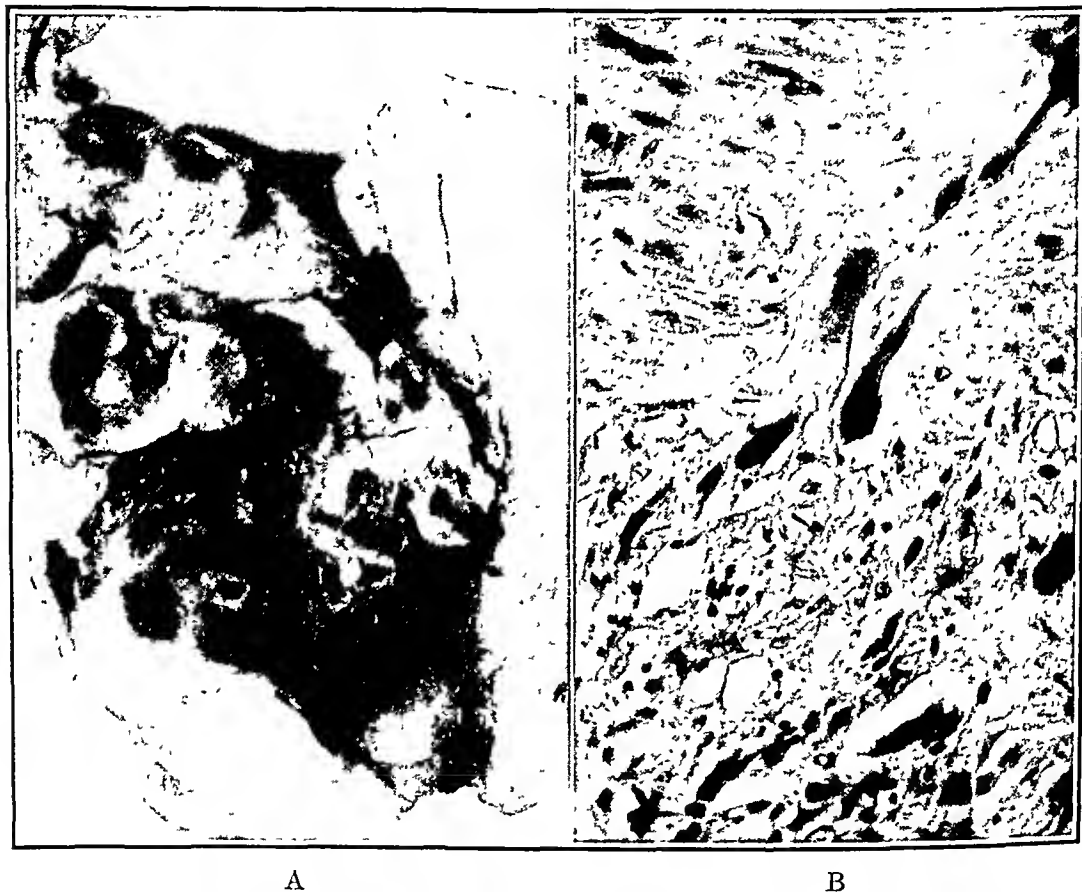


FIG. 381 —Chorionepithelioma showing (A) an infiltration of the myometrium with a hemorrhagic necrotic mass and (B) bizarre cells penetrating deep into the wall. x 100.

The *diagnosis* is based upon the history, uterine curettage, and hormonal alterations. *Treatment* consists of hysterectomy. The *prognosis* is poor, but cures even in the presence of metastases are recorded. Before leaving this subject, two terms ought to be defined. *Syncytioma* is sometimes employed in those tumors that are composed principally or entirely of syncytial cells. *Syncytial endometritis* is used by some authors to indicate normal syncytial elements penetrating the endometrium and myometrium, as frequently seen in post-partum uteri, and by others to indicate scattered neoplastic syncytial cells associated with a leukocytic infiltration. To avoid confusion, both terms should be discarded!

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puberty by invasion of the terminal cartilages with osteogenic tissue. When growth ceases, the two centers of ossification meet and fuse.

ANATOMY

Because of lack of space, it is impossible to even attempt an anatomic and microscopic description of the various bones and bone marrow cells. A few definitions, however, of words used in the text are in order. *Periosteum* covers and forms bone. It is composed of an external layer of dense connective tissue and an inner layer of more loosely arranged collagenous bundles. In growing bones, this layer is lined by osteoblasts. *Endosteum* covers the inner surface of bone that surrounds larger cavities. It is composed of a thin layer of connective tissue that in growing bones is also lined by osteoblasts. *Perichondrium* covers and produces cartilage and is composed of closely packed mesenchymal cells. When it begins to form bone it is called periosteum. *Cancellous bone* is the spongy bone that is present in the marrow cavities. It is composed of interlacing trabecles of bone of varying widths and shapes. *Compact bone* is the dense white grossly solid bone that forms the cortex. The *diaphysis* of a long bone is its shaft. The *epiphysis* is the small piece of bone at the end of the shaft that contains a secondary center of ossification. The *metaphysis* is the distal portion of the diaphysis that is adjacent to the epiphysis.

PATHOLOGY

Congenital Anomalies—Developmental malformations of bones are numerous and varied. Those of the *extremities* consist of *syndactylism*—fusion of or webbed fingers and toes, *polydactylism*—supernumerary fingers or toes, *agenesis*—absence of the phalanges of hands and feet, the metacarpals and metatarsals, wrist, radius, ulna, humerus, forearm, entire upper extremity, smaller bones of the foot, tibia, fibula, femur and entire lower extremity, *hypoplasia*—relative shortening of any of the paired bones or of the entire extremity, *hypertrophy*—relative lengthening of any of the paired bones or of the entire extremity, *bowing*—laterally, anteriorly or medially of particularly the bones of lower extremity, *achondroplasia*—a hereditary deficiency of formation of cartilage of the long bones with immediate ossification. This results in shortening and dwarfism, and *coxa vara*—a progressive decrease of the angle between the neck and shaft of the femur that may ultimately eventuate in a fracture of the neck. The more common abnormalities of the spine consist of *spina bifida*—failure of fusion of the lamina, *scoliosis*—lateral curvature and twisting, and fusion of the vertebra. The only noteworthy anomaly of the *pelvis* is asymmetrical development. Congenital defects of the *thoracic cage* consist of *supernumerary ribs*—cervical or lumbar, *bifid sternum*, and anomalies of the *first rib*, such as rudimentary when it fails to reach the sternum, vertebral and sternal bony portions joined by a ligament, and complete absence

CHAPTER XX

BONES

EMBRYOLOGY

THE progenitors of all mesodermal tissue in the body are *mesenchymal cells*. Closely related to mesenchymal cells, if not identical with them, are *reticulum cells*. Important from the standpoint of the present topic is the fact that both or either of these cells give rise directly to *bone marrow cells*, *chondroblasts*, *osteoblasts* and *fibroblasts*. Each of these daughter cells in turn cannot only revert to their parent cells but they can transform either directly or indirectly into one another. Thus a primitive marrow cell can transform into a fibroblast, a fibroblast back to a primitive marrow cell or to an osteoblast, an osteoblast back to a fibroblast or to a chondroblast, and a chondroblast back to an osteoblast. It is only by bearing this relationship in mind that the complex composition of some of the bone tumors, to be described presently, can be understood.

Cartilage makes its appearance about the fifth week of embryonic life. The mesenchymal cells enlarge, become rounded off to form compact cellular precartilaginous cells, and these with a deposition of intercellular matrix form adult cartilage cells. Further growth occurs by a division of central cells and a production of new matrix and by division from the peripheral perichondrium.

Bone appears about the seventh week of embryonic life. There are two types—membrane and cartilage. *Membrane bones* are the flat bones of the face and cranial vault. They are preceded by a connective tissue membrane in which appear one or more points of ossification. These consist of spicules of bone formed by covering osteoblasts. With laying down of the matrix some of the latter are entrapped to become osteocytes. They are surrounded by clear spaces called lacunae. At the periphery, the periosteum produces parallel plates of compact bone. These form the tables of the cranium while the initial spicules remain spongy and form the diploe. A large portion of the original bone is resorbed in part at least by the action of osteoblasts—which are giant cells consisting of fused osteoblasts and freed osteocytes. *Cartilage bones* are preformed in cartilage. They are transformed into bone by ossification from the perichondrium and by ossification from within. The latter is accomplished first by calcification of the cartilage and then by its destruction, disintegration and disappearance through the erosive action of invading primitive marrow tissue. This arises from the perichondrium. Osteoblasts, which appear in the marrow, then give rise to spicules of bone. Growth proceeds laterally, by deposition of periosteal bone and simultaneous resorption of the center, and longitudinally, by continued production of cartilage and then osseous tissue at the ends of the bones. Secondary centers of ossification or epiphyses are established after birth and before

like skull, scoliosis, twisted thorax and excessive mobility of the joints. Fractures are usually multiple, numerous and provoked by the slightest trauma. They affect any bone but particularly the femur, humerus and tibia, are accompanied by little pain, and usually heal readily. The sclera are blue, and deafness occurs in about one-third of all cases. *Röntgenograms* show irregular formation and calcification of the cranial bones, thinning and porosis of the cortex of long bones, and softening and wedging of the vertebral bodies.

Histologically, the periosteum is thickened. The cortical trabecles are long, slender and form a loose network with the long axis parallel to the long axis of the bone. In the trabecles, osteocytes are relatively increased in number, the matrix is irregular, osteoblasts may be defective or normal, and osteoclasts are depleted. There is no abnormality in the repair of fractures.

Treatment is unsatisfactory. Care to avoid trauma is usually without avail. Braces, casts, open reductions and amputations have all been used to cope with fractures. Hormonal therapy has had no beneficial results.

Inflammations—Inflammation of bone is known as *osteomyelitis*. The infections may be listed as follows: (1) *non-specific*—hematogenous osteomyelitis, exogenous infection following compound fracture, Brodie's abscess, aseptic necrosis, and echinococcus cyst, and (2) *specific or granulomatous*—tuberculosis, syphilis, eosinophilic granuloma, lipid storage diseases, coccidioidal granuloma, Boeck's sarcoid, actinomycosis, blastomycosis, leprosy and granuloma inguinale. Since many of these conditions are similar to those described in other organs and are in addition rare, they will not be considered further.

Hematogenous osteomyelitis as the name implies is an inflammation of bone that comes about by way of the blood stream. Most of the cases when first seen are of the acute type and are caused by pyogenic organisms such as staphylococcus (90 per cent), streptococci and pneumococci. Rarely, the process may be chronic from the start and due to organisms such as the typhoid bacilli. Sometimes, the primary infection in the form of a furuncle, abrasion of the skin, tonsillitis, or a focus in the respiratory, intestinal or urinary tract is detectable but at other times, the source of the bacteremia is not apparent. Factors which usually localize the organisms to the metaphyses (the site of predilection) are said to be the sharp hair-pin curves in the blood vessels at this point which slow the flow of blood, focal thrombi sustained by mild often unnoticed trauma and diminished phagocytic activity in this area as compared with other portions of the marrow. Once bacteria are lodged they multiply rapidly. As they do so, they liberate exotoxins which diffuse into the adjacent bone and there destroy leukocytes and erythrocytes, coagulate plasma and produce more thrombosis. This is brought about a vicious cycle. The destruction of bone and the liberation when leukocytes are disintegrated.

Clinically, the infection is most often found in the lower extremities especially the upper end of the tibia. The peak incidence is in

In addition to the above, two lesions that merit more than passing comment are hereditary multiple exostosis and osteogenesis imperfecta.

Hereditary Multiple Exostosis.—This has *also* been called multiple cartilaginous exostoses, multiple exostoses, diaphysial aclasis, hereditary deforming chondrodysplasia and dyschondroplasia. It is characterized by the appearance of multiple, bilateral and symmetrical, knobby bony and cartilaginous outgrowths from all but the membranous bones of the skull and the tarsal and carpal bones. The *lesions* are particularly common at the site of bone growth or cartilaginous plates and are, therefore, conspicuous in the extremities. The nodules vary in size from mere excrescencies to ones that measure 4 to 5 cm. or more in diameter. They are rounded, tubular or pedunculated. The periosteum of the adjacent bone continues over them and they, therefore, form part of the cortex. In younger patients, the surface is capped with a 2 to 5 mm. layer of hyaline cartilage. In older patients, however, the cartilage is absent and when the protuberances are larger they may be covered with a bursa. *Histologically*, the bulk of the nodule is composed of delicately trabeculated spongy bone in the interstices of which there is a fatty marrow.

Three *theories* submitted to explain the disorder are (1) that tiny pieces of cartilage are pinched off from the margins of the plates, (2) that the lesions arise from the periosteum and (3) that the condition represents an abnormal periosteal and perichondrial activity together with a defective moulding of the bone. The disorder is transmitted through an affected or unaffected female and it is found in males twice as frequently as in females. *Symptoms* usually become manifest between two and fourteen years of age and consist merely as one or more bumps on the skeleton. Later, however, pressure on adjacent tissues interferes with articulation, while dissipation of growth in a lateral direction results in curvature and shortening of the bones and retardation of growth. Deformity of the forearm occurs in about one-third of all cases. *Treatment* is not indicated unless the tumors interfere with function or unless one of them is transformed into a *chondrosarcoma*. The latter occurs in about 10 per cent of the cases.

Osteogenesis Imperfecta.—This is *also* known as fragilitas ossium, brittle bones, blue sclera and otosclerosis, idiopathic osteopsathyrosis, osteitis parenchymatosa chronica, dystrophia periostalis, periosteal aplasia and periosteal dysplasia. Among other classifications it has been divided into a hereditary and non-hereditary type. Its *cause* is unknown, but theoretically, it is considered to be due to an abnormality of osteoblasts, lack of phosphoric acid and phosphatase in the blood, a hereditary defect in the germ plasma or endocrine disturbances.

The disorder affects males and females with equal frequency. *Clinical* manifestations may be so mild as to be barely detectable or they may be so severe as to be incompatible with life. The adult may be normal while the infant may be poorly nourished, short and extremely deformed, presenting a triangular head with parchment-

evidenced by the presence of spicules of osteoid tissue surrounded by osteoblasts

The *diagnosis* of osteomyelitis is ordinarily not difficult if the condition is borne in mind. Sometimes, however, the local manifestations may be obscured by the severe systemic reaction. Important from a differential standpoint are acute rheumatic fever, pyarthrosis, cellulitis and Ewing's tumor. *Treatment* consists of early and intensive antibiotic therapy and chemotherapy. In many instances, this alone will eventuate in a cure. In the remaining few patients, focal collections of pus may necessitate subsequent incision and drainage. Formerly, it was said that once a patient had osteomyelitis he was never cured of the disease. With the advent of antibiotic therapy and chemotherapy, this statement no longer holds true. If treatment can be started early, the *prognosis* is good.

Brodie's abscess is a chronic abscess of bone that is closely related in its genesis to acute hematogenous osteomyelitis. It has a predilection for the metaphysis of long bones, is caused by the same organisms and predominates in males. Its difference lies in the fact that the onset is usually insidious. *Symptoms* ordinarily consist of mild or more severe intermittent pain over the end of one of the bones with gradual enlargement of the affected part. There are frequently local tenderness, swelling, limitation of motion and shortening. Roentgenograms disclose a sharply defined area of decreased density measuring as much as 7 cm in diameter and surrounded by dense bone. *Pathologically*, the center of the cavity is filled with a homogeneous mass of granulation tissue, but as the lesion enlarges it becomes cystic and the pockets are filled with serous or purulent material. The surrounding bone gradually becomes more dense and eburnized. Although the cortex becomes thinned fractures are infrequent. *Treatment* is excision and saucerization of the bony defect together with antibiotic therapy and chemotherapy. The *prognosis* is excellent.

Aseptic necrosis of the epiphyses and of the smaller bones is more common in boys than in girls and predominates between the ages of three or four years and puberty. *Clinical manifestations* may be absent or they may consist of mild or moderate pain, limp, if the bone is weight bearing, and tenderness. *Roentgenograms* of the involved bones and epiphyses disclose a progressive destruction as evidenced by small areas of decreased density followed by fissuring, fragmentation, fuzzy outlines, flattening of the head, shortening and occasionally loose bodies in the joint. *Pathologically*, the process is thought to consist of death of the ossifying focus with fragmentation, absorption and later recalcification or re-ossification. The disease has been described in the following bones: vertebral bodies, carpal and tarsal scaphoid, semilunar, patella, astragalus, coneiform, clavicle, humerus, radius, ulna, metacarpals, iliac crest, symphysis pubis, femur, patella, tibia, tibial tubercle, os calcis and metatarsals. The *synonyms* are epiphysitis, osteochondritis and subchondral necrosis. The *eponyms* unfortunately are many. Some of the more common are Legg-Perthe's disease when it affects the head of the femur, Osgood-Schlatter's disease when the tibial tuberosity,

childhood and adolescence. Trauma is elicited in the history in about one-third of all cases. Symptoms and signs usually occur suddenly and consist of pain in the affected part, fever, chill, maintenance of the limb in slight flexion, tenderness and swelling over the involved area, leukocytosis and frequently, if in the early stages, a positive blood culture. *Roentgenograms* are initially normal and only later do they show an area of bone destruction.

Grossly, as already stated, the early lesion is a small ill-defined abscess in the metaphysics that penetrates into and rapidly destroys the adjacent bone (Fig. 382). It extends in three directions: (1) into the medullary cavity after which it may follow the haversian canals through the cortex to reach the periosteum at one or several points; (2) directly through the cortex of the metaphysis to reach

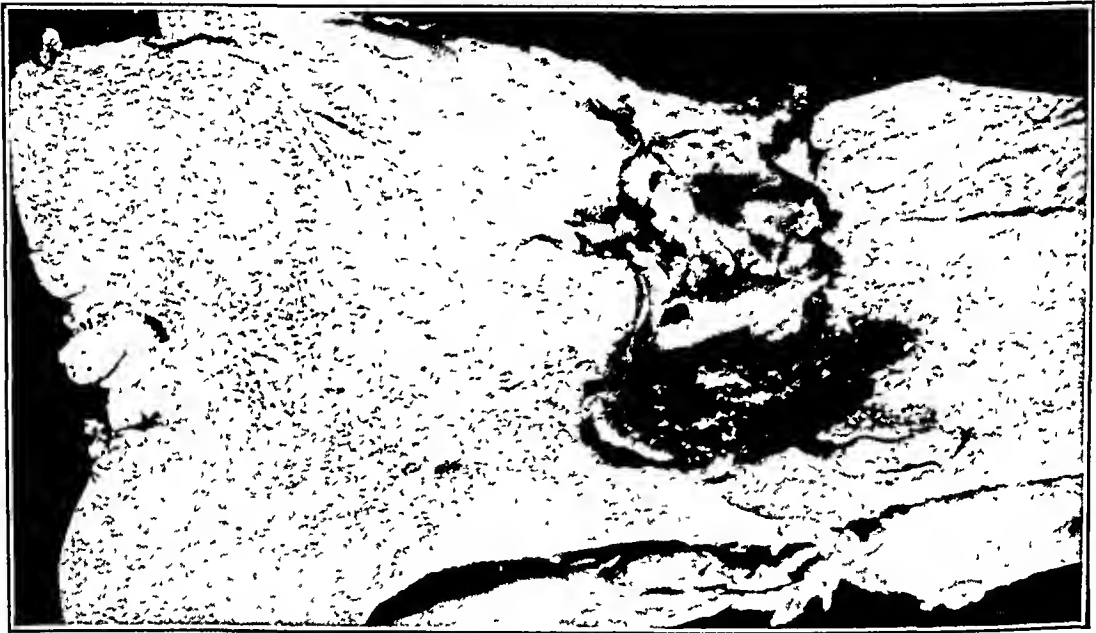


FIG 382.—Osteomyelitis of the metaphysis of the femur Note the sinus tract and the sequestrum

the periosteum near the joint. After the periosteum is reached the abscess may, either spontaneously or as a result of surgical interference, break through the skin to produce one or many sinuses, and (3) through the epiphysis into the joint cavity. Beneath the periosteum the pus spreads up, down and around. The vessels to the bone are thus thrombosed or eroded; the blood supply is cut off, and the bone dies in part or in whole. The dead spicule or mass of bone both in the medulla and in the cortex is called a *sequestrum*. In time, when reparative processes assert themselves, the sequestrum is covered with new bone which is called the *involucrum*. *Histologically*, the picture varies depending upon whether the destructive or the reparative processes predominate. The former consist of leukocytic infiltration, foci of necrosis and dead bone surrounded by osteoclasts. The latter are indicated by the appearance of granulation tissue, fibroblastic proliferation and new bone formation as

lesion in some cases may disclose a central area of caseation surrounded by a grey zone and the entire mass encompassed by hyperemic marrow. In other cases, the involved area consists of encapsulated cyst-like spaces filled with semi-fluid, sometimes gritty material. In each of these, the surrounding bone is destroyed and the cortex is thinned. In still a third variety, the bone is fusiformly enlarged, the periosteum may be raised by subperiosteal new bone formation, and the entire medulla may be filled with dense sclerotic new bone (Fig 383). *Histologically*, as in other areas of the body, the characteristic unit is the tubercle. In some cases, tubercles may be plentiful while in others they may be sparse. In the latter, there is a predominance of tuberculous granulation tissue which is composed of caseating necrotic material, irregularly distributed epithelioid cells and varying proportions of fibroblasts, capillaries and inflammatory cells. *Treatment* consists of immobilization, curettage, incision and drainage, excision, and amputation depending upon type, location and severity of the lesion and the general condition of the patient. The *prognosis* generally is good although in any individual case it may be poor.

Syphilis of the bones may be divided into acquired and congenital types. *Acquired* syphilis occurs at any age after puberty and has no predilection for either sex. The lesion may be single or multiple and it affects in decreasing order of frequency the following bones: tibia, clavicle, skull, fibula, femur, humerus, ribs, ulna and scapula. *Pathologically*, gummatous osteomyelitis with areas of bony destruction is the most common. This is followed by the periostitic type, wherein the periosteum is thickened and dense laminated subperiosteal bone is deposited along the cortex. The least common is the sclerosing variety wherein gummas and syphilitic granulation tissue are inconspicuous and the medulla is filled with dense sclerotic bone.

Congenital syphilis is subdivided into *late hereditary*, which is similar to the acquired infection, and into *early hereditary* types. The latter is present at or develops shortly after birth. *Pathologically*, the most frequent lesion is an *osteochondritis*. This discloses a broad irregular zone of calcification wherein there is an arrest of osteoblastic activity. The columns of cartilage are long and irregular and are separated by syphilitic granulation tissue composed of fibroblasts, perivascular lymphocytes, plasma cells and neutrophils, and later foci of necrosis and fatty degeneration. This tissue is often so exuberant that it may completely split the provisional zone of calcification into an epiphyseal and diaphyseal portion, and may cause separation of the epiphysis. The areas most commonly affected by osteochondritis are lower end of the femur, upper end of the tibia, radius, ulna, metatarsals and phalanges. *Syphilitic periostitis* is next in frequency. It affects the long bones and consists of a diffuse subperiosteal lamellated and radial deposition of new bone. *Syphilitic osteomyelitis* is the least common. It involves the diaphyses of the ulna and radius and less often the phalanges and metacarpals. There are bone destruction, necrosis and gummatous formation.

Kohler's disease when the tarsal scaphoid, Kienbach's disease when the semilunar, and Freiberg's infarction when the second metatarsal. The *cause* of the necrosis is not known but theoretically it has been attributed to endocrine disorders, infection and trauma. In passing, it ought to be pointed out that Legg-Perthe's disease should be differentiated from *slipped upper epiphysis* of the *femur*. This is usually found in rapidly growing, obese and physically active children and produces intermittent pain, limitations of motion, shortening and limp.

Echinococcus cysts of bone are found in about 1 per cent of cases with echinococcus disease. *Symptoms* may consist of a mass or pain. The latter is due to pathologic fracture and frequently to leakage with infection of the surrounding tissues. *Roentgenograms* show a polycystic, sharply defined area of decreased density without

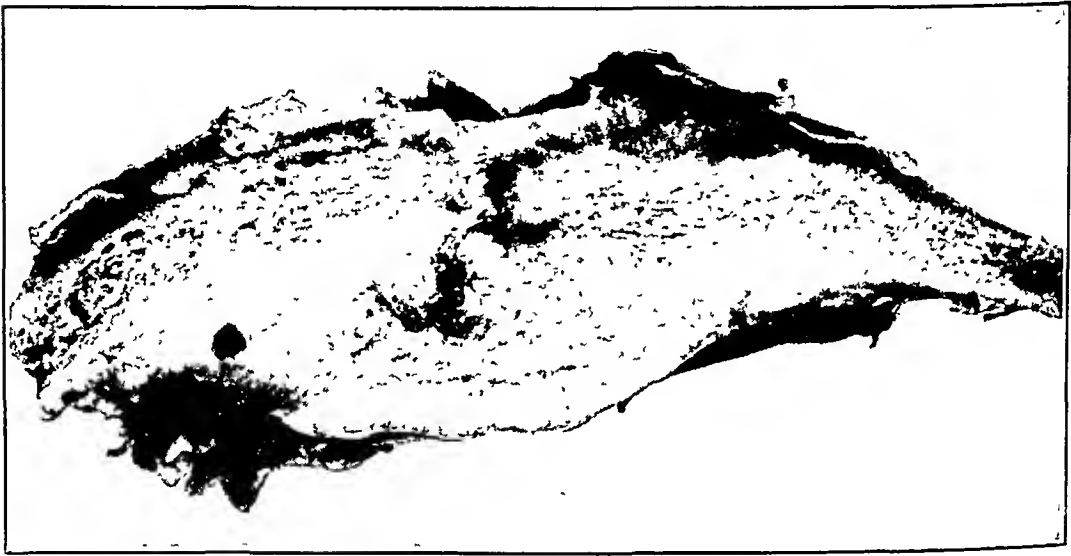


FIG 383 —Tuberculosis of a rib The periosteum is thickened; the cortex is sclerotic; the medulla is filled with new bone, and there is a pathologic fracture.

a surrounding productive reaction zone but with thinning of the cortex. *Pathologically*, the cyst and its contents are similar to those in other organs and described in the chapter on the peritoneum (p. 442). *Treatment* is excision or marsupilization. The *results* are mutilating and leave much to be desired.

Tuberculosis of the shafts of tubular bones and ribs is less common than that of joints. It affects males three times as frequently as females and occurs most often before the age of ten years and after twenty years. It is always secondary to foci elsewhere in the body, particularly the lungs. General *symptoms* include pallor, fatigability, loss of appetite, loss of weight and night sweats, whereas local symptoms consist of pain and swelling of the affected bone. *Roentgenograms* disclose endosteal and medullary sclerosis, irregular bone destruction or circumscribed cystic degeneration. *Pathologically*, the disease usually originates in the metaphysis of the long bones and in the diaphysis of the short bones of the hand and feet. The tibia and the femur are affected most often. Grossly, the

tinoma, a group of disorders that may be called dystrophies and consist of unicameral cyst, osteitis fibrosa cystica (von Recklinghausen's disease), fibrous dysplasia, osteitis deformans (Paget's disease), and myelofibrosis and osteosclerosis, and from distant areas, secondary tumors. In the following paragraphs the benign lesions will be described first in the order listed and these will be followed by a discussion of the malignant ones in the same order.

Osteoma is a benign overgrowth of bone that is similar to hereditary multiple exostosis already described under congenital anomalies. The only difference is that it is a single lesion while the latter is multiple. They have a predilection for the epiphyseal cartilaginous plates and are common about the knee joint, but also occur in the small bones of the hands and feet and in the frontal and



FIG. 384.—Osteochondroma of a proximal phalanx of a finger

maxillary sinuses (Fig. 384). They are hard raised masses that often measure 3 to 4 cm. in diameter. The apex is more or less conical while the base is usually sessile, although sometimes it may be pedunculated. The tumors are a part of the bone, that is, the covering periosteum and perichondrium are continuous with that of the adjacent cortex. The surface of the osteoma is frequently covered with cartilage which in some cases may be abundant enough to justify the term "osteochondroma." The bulk of the tumor is usually composed of cancellous bone and contains fatty marrow. In some cases, however, particularly in tumors of the paranasal sinuses the entire mass consists of compact, ebonized osseous tissue. *Treatment*, consisting of adequate excision, is indicated in all osteomas of the paranasal sinus, for here they are mechanically "malignant." In other locations, they may be left alone unless they interfere with normal function.

Eosinophilic granuloma of bone is a destructive lesion of unknown etiology but thought by some to be related to Letterer-Siwe (a generalized granulomatous reticulo-endothelial disorder that occurs in infants and is rapidly fatal) and Hand-Schüller-Christian diseases. Although trauma and a virus have been suggested as the cause such allegations are without any proof. Two-thirds of the cases occur before twenty years of age and males are affected five times as frequently as females. The lesions are single or multiple and the bones most frequently involved are skull, pelvis, vertebrae, ribs and long bones. *Symptoms* and signs are general and local. The former consist of slight fever, loss of appetite, fatigability, headache, loss of weight and occasionally leukocytosis. Locally, there are pain, swelling, tenderness, and muscle spasm and atrophy. Roentgenograms reveal punched out areas of rarefaction that start in the medulla, and that erode and eventually perforate the cortex. *Grossly*, the areas of destruction are 1 to 4 cm. in diameter and in early lesions are filled with soft, friable yellowish brown or hemorrhagic material. In older lesions, there is a replacement of the contents by grey fibrous tissue and bone. *Histologically*, destruction dominates the initial phases. There are necrosis, hemorrhage and an infiltration with eosinophils, neutrophils, lymphocytes, plasma cells, phagocytes and foreign body giant cells. Later, the dominating cells are large round or polyhedral foam cells with reticulated cytoplasm and relatively small round nuclei. Finally, in the reparative stage even these are replaced with connective tissue and new bone. The *diagnosis* can be made with certainty only by biopsy. *Treatment* is surgical excision, curettage or irradiation therapy. The *prognosis* is good. Some lesions heal spontaneously following a pathologic fracture.

Lipoid storage diseases that affect bones are the same as those that involve the rest of the reticulo-endothelial system. Although the medulla is usually infiltrated histologically, the lesions are not necessarily demonstrable roentgenographically. Postive findings consist of focal or more diffuse areas of decreased density in the medulla with varying degrees of cortical erosion. In Gaucher's disease, the bones most frequently affected are the femur, vertebrae and skull, in Hand-Schüller-Christian's disease, the skull, and in Niemann-Pick's disease, any of the marrow containing bones.

Tumors.—A histogenetic classification of tumors or tumor-like conditions of bones is not entirely satisfactory not only because a single tumor may contain various types of tissue but also because the origin and the exact nature of some of the disorders is not well understood. Despite these shortcomings, however, the following tabulation is offered: from osteoblasts, an osteoma, osteoid osteoma, infantile cortical hyperostoses, hereditary multiple exostosis and osteosarcoma; from chondroblasts, a chondroma, benign chondroblastoma and chondrosarcoma; from fibrous tissue, a fibroma, giant cell tumor and fibrosarcoma; from blood vessels, a hemangioma, hemangioendothelioma and hemangiosarcoma; from marrow cells, a myeloma, Ewing's tumor, the lymphoblastomas and a liposarcoma; from nerves, a neurofibroma; from epithelial inclusions, an adaman-

Grossly, in either case, the adjacent bone is eroded, invaded and thinned. The tumor is white or bluish white and on section may disclose varying degrees of cystic degeneration, calcification and ossification. *Histologically*, the capsule sends septa into the tumor and thus divides it into lobules. The ground substance is hyalin and contains lacunae, wherein lie single or sometimes double or triple small cells. Their cytoplasm is light staining or vacuolated, and the nuclei are relatively small and intensely blue. In areas of myxomatous degeneration, the cells are usually stellate and disclose long processes. *Treatment* of enchondroma is curettage, and of echondroma wide excision. The importance of chondromas lies in the fact that if they are not completely excised they will recur and that ultimately, over a period of five to ten years they often become malignant.

Benign chondroblastoma is a rare tumor that has been called a chondrosarcoma, chondroblastic sarcoma and benign calcifying

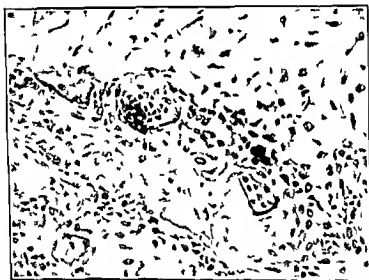


FIG. 380.—Benign chondroblastoma showing chondromatous tissue and multinucleated foreign body giant cells. $\times 100$

chondromatous giant cell tumor. It occurs in the second decade of life and is located in the epiphyses and adjacent metaphysis of the upper end of the humerus, lower end of the femur and upper and lower ends of the tibia. *Clinically*, the joints show pain, swelling, heat and limitation of motion. The tumor itself produces a tender swelling. *Roentgenograms* disclose a round or oval intraosseous area of rarefaction that distends the cortex and sometimes bulges into the joint cavity. It may or may not be trabeculated. *Grossly*, the growth is composed of grey, white, brown or hemorrhagic solid or necrotic tissue admixed with calcareous particles. There may or may not be cysts. *Histologically*, the stroma consists of edematous or mucoid and chondromatous tissue in which are embedded closely packed or more loosely spaced round, oval or polyhedral cells (Fig

Osteoid osteoma is a slowly growing, benign tumor of bone forming mesenchyme. It occurs most frequently in the second and third decades of life and it affects males twice as frequently as females. *Clinical* manifestations consist of pain, exquisite tenderness, and local swelling, erythema and heat. *Roentgenograms* disclose a circumscribed round or oval area that contains small central areas of rarefaction and condensation. At the periphery, there are two zones of sclerosis separated by a zone of rarefaction. The lesion is located subperiosteally, intracortically or intramedullary. The bones that have been affected are tibia, fibula, femur, vertebrae, bones of the face, humerus, ulna, skull, phalanges, patella, calcaneus, talus, tarsal, navicular and ilium. *Grossly*, the periosteum is thickened, edematous and hemorrhagic and the covering new bone is dense and sclerotic. The tumor itself is mottled red brown and grey and is composed of gritty friable or more solid tissue. *Histologically*, the center is composed of cellular vascular embryonic tissue containing osteoblasts, islands of osteoid tissue surrounded by osteoblasts, and foci of calcified osteoid tissue encompassed by both osteoblasts and osteoclasts. About the periphery, the osteoid and calcified tissue is more abundant and beyond this the mesenchyme again prevails. *Diagnosis* is made roentgenographically and by biopsy. *Treatment* is local excision. The *prognosis* is good for the lesion does not recur if it is completely excised.

Infantile cortical hyperostoses is apparently a self-limited disease that starts in the age period between three weeks to twenty months after birth. The disorder consists of a subperiosteal cortical hyperplasia of bone and a swelling of the overlying soft tissues. In some cases, there are, in addition, fever, hyperirritability, pseudoparalysis, dysphagia, pleurisy, anemia, leukocytosis, increased sedimentation rate and high serum phosphatase. The bony lesions, are, as a rule, multiple. The bones that have been described as affected are the mandible, clavicles, calvarium, scapulas, ribs and long bones of the extremities. The course of the disorder is unaltered by any known form of therapy.

Chondromas are benign tumors of cartilage that arise in areas where cartilage is normally found, from misplaced cartilaginous rests as in shafts of bones, and less frequently from the periosteum itself. They affect both sexes with equal frequency and are discovered, as a rule, from the second to the sixth decades of life. Symptoms consist of a local swelling when the tumor protrudes externally (ecchondroma), and may be absent or consist of swelling and pain due to pathological fracture when the tumor grows intra-osseously (enchondroma). *Roentgenograms* disclose a circumscribed area of decreased density which may, however, contain irregular foci or deposits of increased density if calcification or ossification is present.

Enchondromas may be multiple, especially when they affect the small bones of the hands and feet, or they may be solitary. The latter may also affect the phalanges and metacarpals and metatarsals, but, in addition, they frequently involve the femur and humerus. *Ecchondromas* are usually solitary, lobulated, well encapsulated and measure as much as 20 cm. or more in diameter.

Giant cell tumor of bone may be considered as a fibroma of bone that is unusually rich in foreign body giant cells. It characteristically occurs after twenty-one years of age and has no predilection for either sex. Symptoms frequently consist of pain and swelling and, as in most other tumors of bone, are erroneously attributed to trauma. Roentgenograms reveal an eccentric, sharply circumscribed, trabeculated area of rarefaction located primarily in the epiphysis and secondarily extending to the capsule and into the metaphysis (Fig 386A). The sites of predilection for the tumors are the ends of the long bones, especially those about the knee but they may also occur in the mandible, maxilla and other bones.

Grossly, the involved portion of the bone is asymmetrically expanded (Fig 386B). The cortex is thin and may even be perforated in one or more areas. Likewise the articular cartilage may be pushed

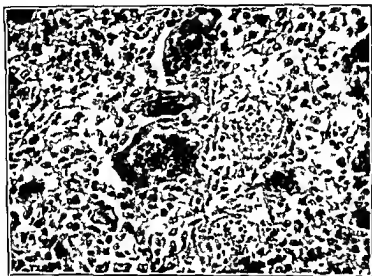
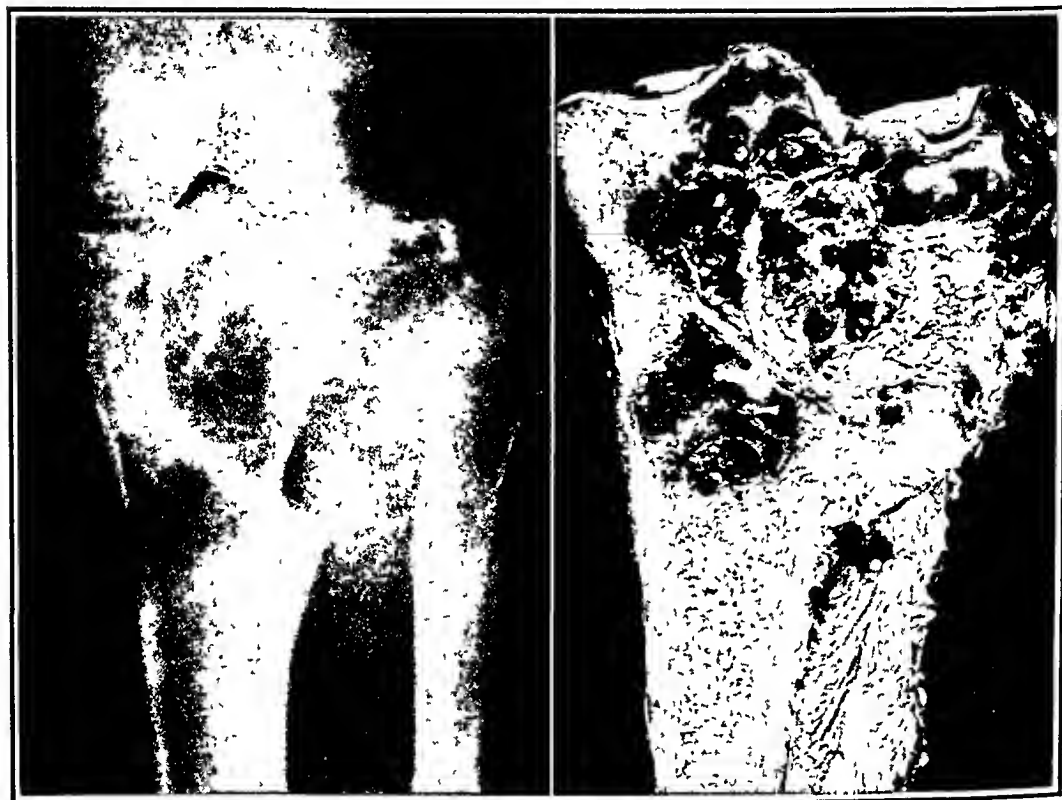


FIG 387—Benign giant cell tumor from same case as illustrated in figure 386. There are present plump fibroblasts and numerous multinucleated giant cells of the foreign body type. $\times 100$

ahead of the neoplasm into the joint cavity. Cut surfaces of young tumors are usually diffusely grey, but as the growths become older they attain a mottled grey, brown, hemorrhagic, orange and yellow appearance. Foci of necrosis are the rule in larger tumors. They frequently become cystic and are filled with serous hemorrhagic or brown fluid. Histologically, the fundamental element is fibroblastic connective tissue (Fig 387). Its structure varies considerably from rather loose and cellular, to dense and somewhat sclerotic. In the former, the cells are ill-defined, the cytoplasm is moderate in amount and eosinophilic, and the nuclei are plump, oval or more elongated and rather deeply stained. Thin walled capillaries are not usually abundant but in areas of hemorrhage there are, as a rule, large spaces lined by tumor stroma and filled with blood. Large multinucleated giant cells of the foreign body type may be sparse or numerous. They consist of an abundant amount of cytoplasm and numerous

385). They contain a moderate amount of cytoplasm and a large round or oval deeply stained nucleus. Multinucleated giant cells of the foreign body type are often quite numerous. The tumor also contains foci of necrosis and irregular patches of hyalin and calcified cartilage surrounded by collagenous connective tissue. *Treatment* consists of a thorough curettage. The *prognosis* is good.

Fibroma of bone is similar to a fibroma in extraosseous tissue. In its pure form it contains no bone and is located within the metaphyses of the long bones, particularly those of the lower extremity. It has no predilection for either sex and is found before the twentieth year of life. *Symptoms* are absent or consist of pain and swelling, and



A

B

FIG 386 — Benign giant cell tumor of the tibia showing a roentgenogram, A, and gross section, B. Each discloses destruction of bone, trabeculation and thinning of the cortex.

are usually attributed to trauma. The involved area is, as a rule, tender. *Roentgenograms* reveal an eccentric, lobulated expanding area of rarefaction that erodes the cortex. *Grossly*, the overlying bone is thin. The tumor usually measures less than 5 cm. in diameter. Externally, it is lobulated and the individual lobules are surrounded by dense or spongy bone. The growth is firm and on section discloses a homogeneously grey or mottled grey brown and yellow surface. *Histologically*, it consists of intertwining bundles of cellular or collagenous fibrous tissue in which there are moderate numbers of capillaries, varied amounts of hemosiderin, scattered foreign body giant cells and foci of foam cells. *Treatment* consists of a thorough curettage or in some cases excision. The *prognosis* is excellent.

the lumen. *Histologically*, the lining is composed of connective tissue that is thin in some areas but thicker and more vascular in others (Fig 388). It contains brown granules of hemosiderin, osteoid tissue and new bone. Attached to its inner surface there are often collections of fibrin which contain cholesterol crystals and scattered foam cells. The encasing bony tissue is loose, vascular and reveals a few giant cells of the foreign body type. *Treatment* consists of curettage and filling the cavity with bone chips. The *prognosis* is excellent.

Osteitis fibrosa cystica is also known as hyperparathyroidism and von Recklinghausen's disease of bone. It is due to hyperactivity of the parathyroid glands, as a result of which the calcium is withdrawn from the bones and the bones become soft and deformed.



FIG 388—Unilocular cyst showing cellular connective tissue foam cells and osteoid and new osseous tissue. $\times 100$

The clinical features of the disorder have been considered in Chapter VI in connection with the parathyroid glands. *Roentgenographically*, there is general decalcification of the skeleton with areas of cyst formation and usually considerable deformity (Fig 389). Because of excessive excretion of calcium, renal stones are common. *Grossly*, the bones are fusiformly and irregularly expanded. The cortex is thin and fractures are common. Cut surfaces disclose areas of yellow marrow embedded in gritty, gelatinous, rather soft tissue. Scattered throughout, there are tiny or larger cysts that are traversed by fibrous trabecles and are empty or filled with gelatinous blood-tinged material. The lining of the cysts is usually grey and smooth. *Histologically*, the subperiosteal bone is thin, contains fibrous marrow and discloses areas of osteoid tissue covered with osteoblasts. At the periphery, there are also a few giant cells of the foreign body type (osteoclasts). The marrow reveals a depletion of the trabecles, a replacement with closely packed or more

centrally placed round or oval evenly stained nuclei. Other elements that are encountered usually in variable and inconspicuous degrees are brown hemosiderin pigment, foam cells, occasionally spicules of osteoid tissue and rarely foci of cartilage.

The *diagnosis* is made from a history which indicates a slowly growing tumor, from the roentgenograms and from a biopsy. *Treatment* of choice is curettement or excision. Irradiation is used for inaccessible areas such as the vertebral bodies. The *prognosis* is generally good but if the tumor is not completely eradicated it must be guarded for the neoplasm can and does, at times, become malignant.

Benign hemangiomas of bone occur at all ages and affect both sexes with equal frequency. In the approximate order of frequency, the bones involved are vertebrae, skull, pelvis, shoulder, long bones of the extremities and small bones of the hands and feet. *Symptoms* may be absent or because of bone destruction, they may consist of pain, deformity and paralysis from pressure upon the spinal cord. *Roentgenograms* differ according to the bone affected. The vertebrae show an absorption of some and thickening of other bony trabecles; the flat bones disclose a "sun ray" appearance, and the long bones reveal a cystic trabeculated defect. *Grossly*, the growths are spongy and hemorrhagic. *Histologically*, they are usually of the cavernous variety and, rarely, of the capillary type. *Treatment* is excision or irradiation. The *prognosis*, as a rule, is good.

Neurofibromatosis of bone is said to occur in about 7 per cent of the cases with the generalized form of the disease. The latter has been described in Chapter I. In bones the tumors arise from nerves in the periosteum, in the cortex and in the medulla and the osseous erosions will, therefore, differ accordingly. Aside from the presence of the tumor itself, the bones tend to become more porous and softer; some through stimulation increase in length, whereas others because of destruction of the epiphysis are stunted; spontaneous fractures and pseudarthrosis develop, and deformities, particularly scoliosis, are common. The lesions both grossly and microscopically are similar to those in other organs.

Unicameral cyst, as the name implies, is a solitary cyst of bone. While formerly it was considered as a type of osteitis fibrosa cystica, giant cell tumor or an encapsulated hemorrhage, it is now regarded as a distinct entity that results from a local abnormality of development. The defect starts near the epiphysis and with growth of the bone gradually creeps towards the center of the diaphysis. It is usually discovered between the ages of infancy and puberty. The bones affected are the humerus, femur, tibia, ulna and radius. *Roentgenographically*, the lesion appears as a solitary, sharply delineated, sometimes trabeculated area of rarefaction. The diameter of the medulla becomes expanded and the inner surface of the cortex is irregularly eroded. *Grossly*, the cortex is thinned so that the cyst may be seen through it. The cyst wall is, as a rule, grey, smooth on its inner surface, and delicate. It contains straw colored or blood-tinged fluid or frankly clotted blood. The trabeculated appearance seen in roentgenograms is due to partial bony sept

in the long bones occur in the diaphysis, but do not invade the epiphyseal line or the articular cartilage (Fig 390A) Trabeculations are, as a rule, not prominent and there is little or no reactive bone peripherally

Grossly, the cortex is expanded or not, but it is always thin The defects in the bone measure as much as 8 cm in diameter They are filled with moderately firm or gelatinous greyish white tissue which may be rich in capillaries and often shows focal hemorrhages, yellowish areas of degeneration and small cysts Some tumors may

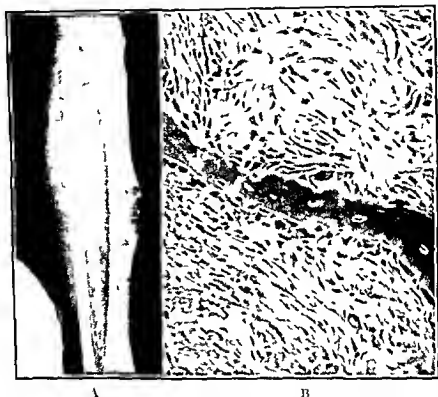


FIG 390—Monostotic fibrous dysplasia of the tibia in a girl eighteen years of age The roentgenogram (A) discloses a trabeculated area of decreased density in the diaphysis and the photomicrograph (B) reveals loose connective tissue and a spicule of new bone $\times 100$

be gritty due to spicules of bone and pieces of cartilage Histologically, the basic tissue is fibrous (Fig 390B) It contains irregularly distributed thin-walled capillaries, hemorrhages and hemosiderin, nests of giant cells of the foreign body type, trabeculae of new bone, small pieces of hyaline cartilage, and occasionally, collections of foam cells

The diagnosis can only be made from a consideration of the history, roentgenograms and biopsy Treatment is symptomatic when the disease is disseminated It consists of curettage and filling the defect with bone chips when it is monostotic The prognosis is excellent in single lesions and is good to fair in multiple lesions

edematous fibrous connective tissue, dilated capillaries, hemorrhages, free and engulfed hemosiderin pigment, and numerous osteoclasts that are frequently grouped into small colonies. *Treatment* consists of extirpation of the enlarged parathyroid gland or glands. If the disease is recognized relatively early, the *prognosis* is good, otherwise it is poor. The *cause of death* is renal insufficiency or marasmus.

Fibrous dysplasia represents a congenital anomaly of bone forming mesenchyme. It occurs in the monostotic and polyostotic forms and has *also* been called *osteitis fibrosa cystica disseminata*, *osteodystrophia fibrosa*, *fibrocystic disease of bone*, *Allbright's disease* and a form of *von Recklinghausen's disease of bone*. When the



FIG 389 —Osteitis fibrosa cystica There are widespread destruction and deformities of the bones and a calculous in the right kidney

disease affects infants and children it tends to be *more severe* and is then accompanied by pigmentation of the skin, precocity in females, premature skeletal growth and maturation, abnormalities of the heart and kidneys, and multiple lesions and deformities of bones (*Allbright's disease*). When the disease is first recognized in adults or older children it is *less severe* and often involves only one bone. Symptoms then consist of swelling, pain and limp, due to a pathological fracture if the bone is weight bearing. The blood serum calcium and phosphorus are normal. The bones most often affected are the femur, pelvis, tibia, humerus, radius, ulna, small bones of the hands and feet, skull, ribs, maxilla and clavicle. *Roentgenograms* disclose sharply circumscribed areas of decreased density that

in the long bones occur in the diaphysis, but do not invade the epiphyseal line or the articular cartilage (Fig 390A) Trabeculations are, as a rule, not prominent and there is little or no reactive bone peripherally

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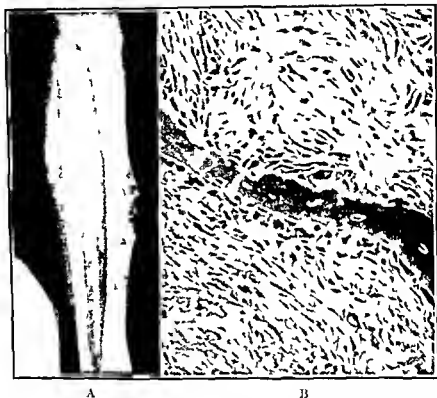


FIG 390—Monostotic fibrous dysplasia of the tibia in a girl eighteen years of age The roentgenogram (A) discloses a trabeculated area of decreased density in the diaphysis and the photomicrograph (B) reveals loose connective tissue and a spicule of new bone $\times 100$

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The diagnosis can only be made from a consideration of the history, roentgenograms and biopsy Treatment is symptomatic when the disease is disseminated It consists of curettage and filling the defect with bone chips when it is monostotic The prognosis is excellent in single lesions and is good to fair in multiple lesions

Osteitis deformans, also called *Paget's disease* of bone, has no predilection for either sex and usually occurs after the age of fifty years. *Symptoms* consist of pain and tenderness over the affected bones and later deafness. Elevation of the serum alkaline phosphatase is the only chemical change in the blood. The following deformities in advanced cases are rather characteristic; enlargement of the head and face, decrease in stature, semi-crouched position, large overhanging upper extremities, and bowing of the femurs laterally and the tibiae anteriorly. More frequently, however, the disease is

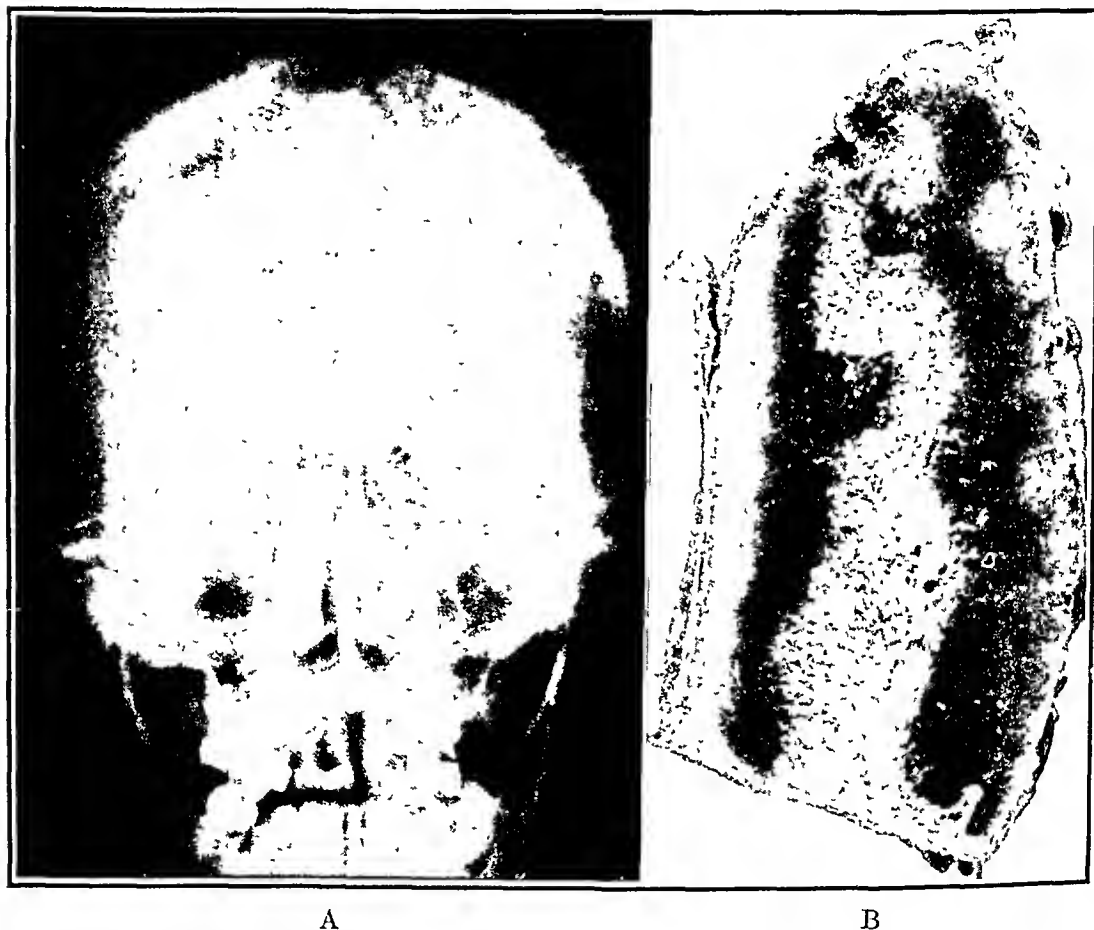


FIG 391.—Osteitis deformans The roentgenogram (A) shows the typical mottled, "cotton-wool" appearance and the gross specimen (B) reveals a great thickening of the cortex of the skull.

limited in scope and is accompanied by no externally apparent abnormalities. The bones affected in the approximate order of frequency are the sacrum, pelvis, vertebra, femur, skull, tibia, humerus, radius, fibula, and metacarpals. *Roentgenograms*, although characteristic, may be confused with metastatic carcinoma of the prostate. They disclose a thickening of the cortex and a replacement of the usual shadow with one of mottled, fuzzy and so-called cotton wool appearance (Fig. 391A).

Grossly, the bones are, as a rule, greatly thickened but they are light in weight and porous (Fig. 391B). The thickening is primarily in the cortex, grows outwardly and only secondarily does it encroach

upon the medulla. Early in the course of the disease the bones are unduly soft but later they become calcified and hard. *Histologically*, the process is one of bone absorption, fibrous tissue replacement and abundant new bone formation. The latter, however, is not normal. It consists of an irregular deposition of osteoid tissue with irregular calcification to produce what is aptly described as a mosaic pattern (Fig 392). Osteoblasts may cover the new trabecles, and foreign body giant cells (osteoclasts) may be moderate in number or sparse. The interstices are filled with loose, well-vascularized connective tissue.

The *diagnosis* is usually apparent from a study of roentgenograms and is readily confirmed, if in doubt, by biopsy. *Treatment* is symptomatic and quite ineffective. *Complications* consist of nerve deafness and optic atrophy, pathologic fractures in 15 per cent of



FIG 392—Osteitis deformans showing the typical mosaic pattern. From the bone illustrated in figure 391B.

the cases, and sarcomatous (osteosarcoma, chondrosarcoma and fibrosarcoma) transformation which is reported as occurring in 2 to 9.5 per cent of all cases. In general, however, the *prognosis* is good and the life span is not shortened.

Myelofibrosis and osteosclerosis occur secondarily in many diseases of bone and bone marrow, but the use here is restricted to the idiopathic generalized type, that is, the one in which a causative agent has not been discovered. *Clinically*, there are progressive weakness, splenomegaly, bone pains, refractory anemia, thrombocytopenia, leukopenia, presence of a few immature cells in the peripheral blood and a failure to obtain fluid upon performing a sternal puncture.

Pathologically, there are a diffuse or focal proliferation of endosteal bone, an absence of osteoclasts, a hypoplasia and then a gradual fibrosis of the marrow, and a compensatory development of hematopoiesis in the liver, spleen, lymph nodes and occasionally other

organs. The *diagnosis* is suspected from clinical studies and the failure to obtain fluid by sternal puncture. It is confirmed by biopsy from the sternum. *Treatment* is palliative in the form of blood transfusions. Spontaneous remissions do occur, but the ultimate *prognosis* is poor.

Osteosarcoma as used here indicates a primary osseous tumor that is composed of osteoblasts and their precursors and that actually or potentially produces bone. In contrast the term *osteogenic* indicates a tumor that arises in bone and includes osteosarcoma, chon-



FIG. 393 —Osteoblastic osteosarcoma of the femur. The roentgenogram (A) shows destruction of the cortex and medulla by radio-opaque tumor and elevation of the periosteum with a typical sunburst appearance. The gross specimen (B) confirms these findings.

drosarcoma and fibrosarcoma. The *cause* of osteosarcoma, as in other tumors throughout the body, is not known. Evidence has accumulated, however, to indicate that one precipitating factor in some instances is radioactive material. The literature contains at least two dozen case reports of fibrosarcoma and osteosarcoma developing in bones that were in the path of roentgen rays, administered for a benign condition or in people who have ingested radioactive material (dial workers). Similar lesions have been produced in experimental animals by the use of roentgen rays, radium or radium chloride. Osteosarcoma is a tumor of youth, for it occurs most often

between the ages of fifteen to twenty-five years. Rarely, it is seen in older patients and in many of these it probably arises on the basis of a preceding osteitis deformans. *Clinically*, the usual sequence of events is trauma, pain, tumor and dysfunction. Systemically, there are often fever and leukocytosis and terminally, loss of weight. In order of frequency, the bones most often affected are the lower end of the femur, upper end of the tibia, larger bones of the upper extremities, fibula, and less commonly, ribs, vertebrae and pelvis. Roentgenographically and pathologically, osteosarcoma is usually divided into two types—osteoblastic and osteolytic.

Osteoblastic osteosarcoma ordinarily arises from the periosteum that covers the diaphysis. *Roentgenographically*, it is seen as a fusiform swelling of the diaphysis just proximal to the epiphyseal line (Fig. 393A). The mass gradually tapers towards the mid shaft. The

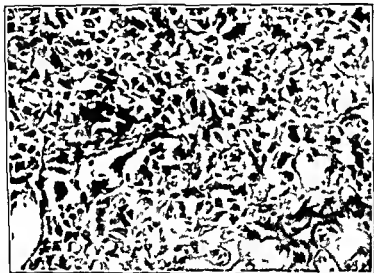


FIG. 394—Osteoblastic osteosarcoma. Same case as illustrated in figure 393. There are bizarre osteoblasts and osteoid tissue. $\times 100$

periosteum is elevated and spicules of new bone are formed at right angles to the main axis of the bone to produce the characteristic sunburst appearance. The cortex and medulla are also infiltrated with radio-opaque tumor tissue. *Grossly*, the findings seen roentgenographically are confirmed (Fig. 393B). The external surface is usually well-encapsulated by a periosteum that is continuous with that of the mid-shaft. Between the periosteum and the old cortex, tumor tissue is deposited and from here, it infiltrates the cortex and extends into the medulla. In its typical form, the growth is partly osseous and, therefore, quite firm. At the periphery, the spicules are clearly seen to be arranged at right angles to the main mass thus accounting for the sunburst appearance. In other tumors, however, there is little or no bone and the entire mass is composed of soft greyish white glistening brain-like tissue. Necrosis and hemorrhage are not apparent. *Histologically*, too, the tumors vary. On the one

hand, there is an abundance of osteoid and osseous tissue and few osteoblasts and primitive mesenchymal tissue (Fig. 394). On the other hand the reverse is true. When the bony elements are in abeyance there may be present scattered small irregular pieces of primitive cartilage but the bulk of the neoplasm consists of large sheets of round, oval, polyhedral and bizarre cells with ill-defined borders and often with long proloptasmic processes. The cytoplasm is scanty, moderate or abundant and oesinophilic or slightly basophilic. The nuclei are round, oval or irregular and intensely hyperchromatic. Mitoses may be numerous and often several nuclei are piled up within a single cell to produce grotesque giant tumor cells.



A

B

FIG 395.—Osteolytic osteosarcoma of the humerus. Roentgenogram (A) shows complete destruction of the upper end of the bone. Gross specimen (B) shows the destructive hemorrhagic tumor mass.

The stroma in such instances is scanty and contains numerous thin walled capillaries. Foreign body giant cells or osteoclasts may be seen but they are usually not numerous.

Osteolytic osteosarcoma is often referred to as malignant bone cyst or aneurysm and is much less frequent. In contrast to the osteoblastic type, it originates in the medulla of the metaphysis and rapidly destroys all the surrounding tissue. *Roentgenograms* are not characteristic. They reveal a rapidly erosive lesion that destroys the entire medulla of the metaphysis, breaks through the epiphyseal line into the epiphysis, eats away the cortex, produces little expansion of the bone, is attended by little or no new bone formation, and is often accompanied by a pathological fracture (Fig. 395A). *Grossly*, these findings are confirmed. The tumor is confined by the

peri-osseous muscles, fascia and tendons or by a mere shell of a cortex with overlying periosteum (Fig 395B) Beneath this the tissue is extremely hemorrhagic It consists of varying amounts of fibrous-like tissue separated by pools of blood Often the entire central portion is converted into a large cyst that is filled with fluid and coagulated blood mixed with tumor The growth extends from the metaphysis into the epiphysis *Histologically*, the most outstanding feature is the presence of lakes of blood separating trabecles of tumor tissue without a surrounding endothelial lining (Fig 396) The neoplastic cells are confluent or sharply demarcated and are round, oval or spindle in shape The cytoplasm is moderate in amount and eosinophilic The nuclei are round, oval, spindle or bizarre and intensely hyperchromatic Mitoses are often numerous, and grotesque multinucleated tumor cells are scattered throughout



FIG 396—Osteolytic osteosarcoma Same case as illustrated in figure 395 There are diffusely extravasated erythrocytes, hemosiderin plump bizarre neoplastic cells and giant cells of the foreign body type $\times 100$

Multinucleated foreign body giant cells or osteoclasts are usually abundant but osteoid tissue is poorly developed and sparse

Osteosarcoma *spreads* by direct extension into the soft tissues and into the adjacent medulla Distant metastasis is ordinarily by the blood stream and the organs usually involved are the lungs and liver Metastasis to other bones is rare and extension to the draining lymph nodes does not occur The *diagnosis* can be made with certainty only by biopsy While the roentgenograms are characteristic they are not pathognomonic for the same sunburst appearance can be produced by any tumor either primary or secondary that raises the periosteum *Treatment* consists of early amputation or disarticulation if the tumor affects the extremities, and wide excision if it is in other bones Irradiation therapy is of no avail If the lesion is a true osteosarcoma, the *prognosis* is poor Although the

five year survival rates are listed as ranging from 5 to 10 per cent, none of the cases that I have seen have survived longer than twelve months.

Chondrosarcoma most frequently arises as a malignant transformation of a chondroma, although, on rare occasions, it is a malignant tumor from the start. The usual story is that a tumor had been present for many years and then suddenly it began to grow rapidly, or that the lesion had been removed one or several times and with each recurrence, it grew more rapidly and more extensively. Chon-

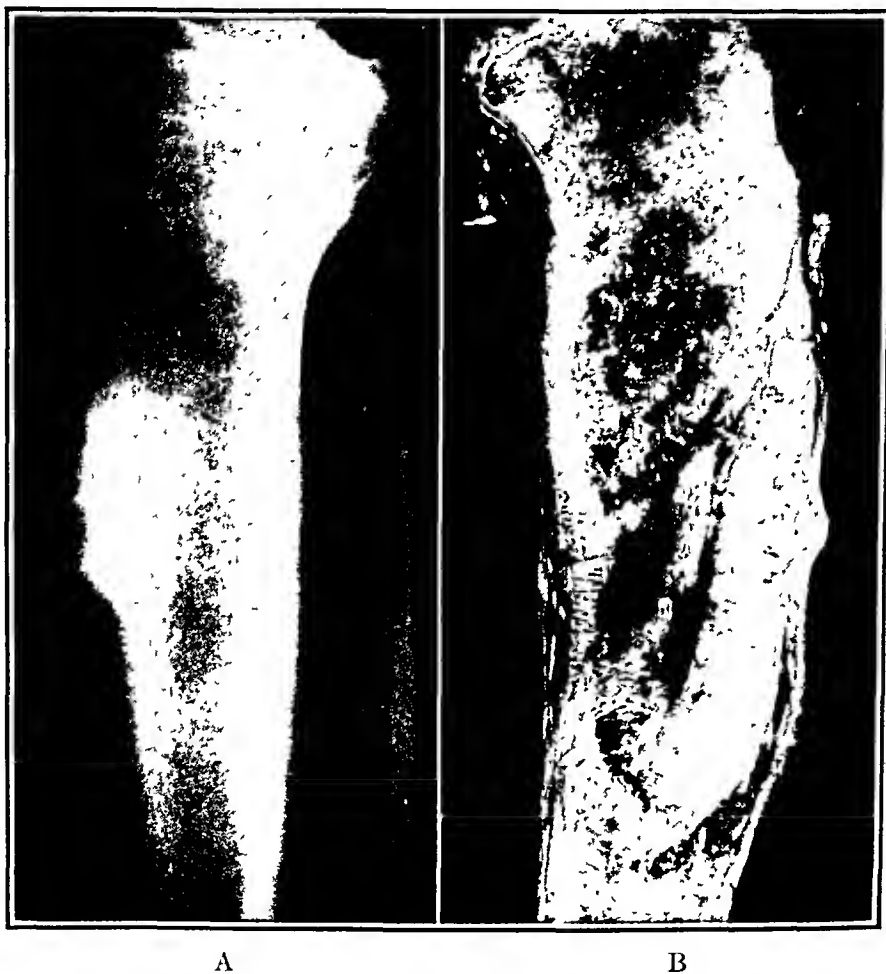


FIG 397.—Chondrosarcoma of the tibia. The roentgenogram (A) shows a partially calcified tumor mass. The gross specimen (B) reveals a periosteal mass that is infiltrating the cortex and medulla.

drosarcoma affects both sexes equally and, although it may be present in the second decade of life, it is more frequent after thirty years of age. *Clinically*, there are tumor, pain and sometimes functional disability. The bones most frequently affected are the femur, tibia, ilium, ribs, scapula, sternum and humerus. *Roentgenograms* reveal an irregularly defined shadow of lesser density than normal bone but containing centrally irregularly mottled and calcified areas (Fig. 397A). Sometimes, however, the latter may be absent.

Grossly, the tumor varies in size from a few to 30 cm. or more. It is sharply circumscribed or ill-defined and hard. Cut surfaces are

frankly cartilaginous, but may contain foci of calcification and ossification (Fig 397B) At other times, the entire tumor is grey, gelatinous, myxomatous and even cystic In the latter, pathological fractures are common *Histologically*, the tumor may differ little from an ordinary chondroma and may, therefore, be extremely difficult to diagnose Usually, however, if enough sections are made its malignant nature is readily apparent In frankly malignant neoplasms, the cells are more numerous, they are large and irregular, the lacunae are filled with one, two or more cells, the cytoplasm is abundant, reticulated or vacuolated and sometimes basophilic, and the nuclei are large, bizarre, plump and intensely hyperchromatic (Fig 398) The matrix may be hyalin or myxomatous When the lesions are more anaplastic, the cells tend to lose their chondroblastic potentialities and then appear as masses of mesenchymal or



FIG 398—Chondrosarcoma showing large and small extremely bizarre cells set in a hyalin matrix $\times 400$

reticulum cells Frequently, in chondrosarcomas, there are foci of bone formation While ordinarily they are quite regular, at times these areas are indistinguishable from foci of osteosarcoma *Spread* of chondrosarcoma is by local extension up and down the medulla and into the adjacent tissue, by blood stream to the lungs and liver, and less often by lymphatics to the draining lymph nodes

The *diagnosis* is made from the history, roentgenograms and always from a biopsy *Treatment* is amputation above the proximal joint if the lesion is on an extremity, and wide excision if it is elsewhere Irradiation is of no value If seen early and treated correctly the *prognosis* should be good, for the tumor, as a rule, remains localized for many months

Fibrosarcoma of bone is no different than fibrosarcoma elsewhere The lesions, as a rule, occur after the age of thirty years and although they may be found in flat bones the site of predilection is a tubular

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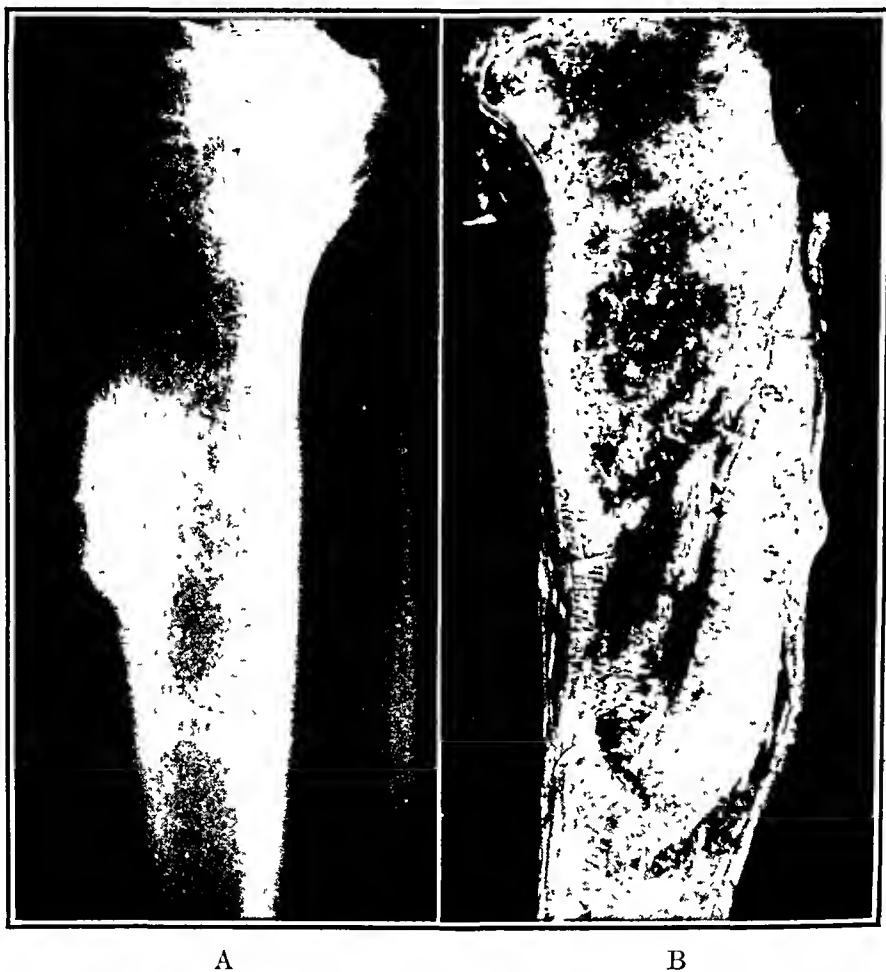
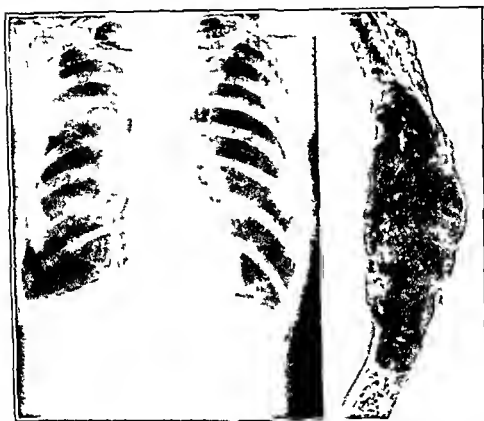


FIG 397 —Chondrosarcoma of the tibia. The roentgenogram (A) shows a partially calcified tumor mass. The gross specimen (B) reveals a periosteal mass that is infiltrating the cortex and medulla.

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are usually single but they may be multiple and they occur most frequently in long bones. *Roentgenograms* reveal rarefaction, destruction, cystic expansion and, rarely, bone formation in the affected area. *Treatment* has been amputation, wide excision and irradiation. The *prognosis* is guarded for many of the lesions are either multicentric in origin or metastasize to other bones and organs.

Myeloma is a heterogeneous group of tumors that arises from marrow cells. By far the greatest number of cases are of the plasma



A

B

Fig. 400.—Multiple myeloma. Roentgenogram (A) discloses an osteolytic mass in the sixth left rib, the seventh right rib and the upper portion of the sternum. The latter bulges on both sides of the mediastinum. The gross specimen (B) represents the destroyed sixth left rib. The rib is fusiformly dilated and all but the periosteum is destroyed by a hemorrhagic mass.

cell variety (plasmacytoma), but cases representing most of the other series of cells have also been described. These consist of the myelocytic, lymphocytic, erythrocytic, megakaryocytic and hypocytic varieties. Since the latter are rare, and, in fact, their very existence being doubted by some authors, the following remarks pertain to the *plasma cell variety*. The disease is found beyond the age of forty years with an average in the sixth decade of life and it is three times as frequent in men as it is in women. The clinical manifestations consist of pain and occasionally tumors and tenderness over

bone. They arise in the periosteum, cortex, endosteum or medulla and destroy the surrounding bone. *Roentgenograms*, therefore, disclose an expanding purely osteolytic lesion. There may or may not be a surrounding zone of sclerosis. *Grossly*, the tumor is fairly well circumscribed but not encapsulated. Its dominant location will depend upon its point of origin. Eventually, however, the medulla, cortex, periosteum and even adjacent tissues are infiltrated with grey, glistening, moderately firm neoplastic tissue that may or may not show foci of necrosis, liquefaction, cyst formation, and hemorrhage (Fig. 399). *Histologically*, the neoplasm is composed of spindle, stellate, oval or bizarre neoplastic cells with scanty or moderate amount of cytoplasm and oval, spindle, or irregular hyper-

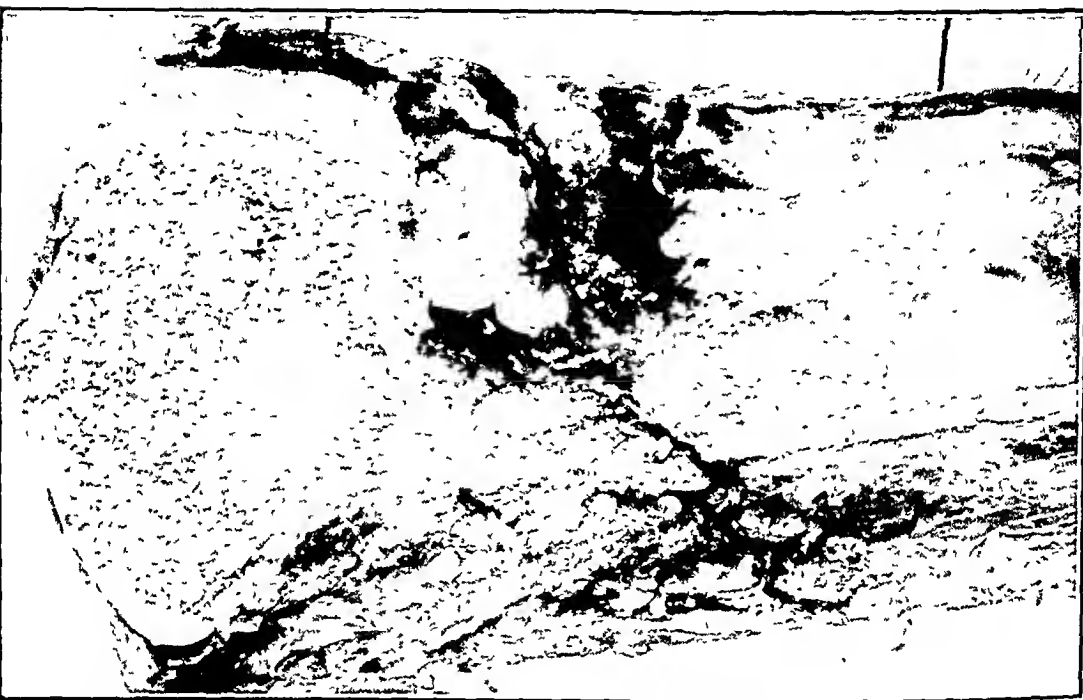


FIG. 399 —Fibrosarcoma of the tibia. The medulla, cortex, periosteum and extra-osseous tissues are infiltrated with soft, grey, brain-like tissue. There is also a pathologic fracture.

chromatic nuclei. It has the same variations in structure as fibrosarcoma elsewhere (see Chapter I). Frequently, it contains foci of calcification, bone and cartilage. The *diagnosis* can only be made by biopsy. *Treatment* is amputation or wide surgical excision if amputation is not possible. The *prognosis* is better than for any other malignant tumor of bone.

Hemangioendothelioma and hemangiosarcoma are malignant vascular tumors of bone. The literature on the subject is quite confused. Some authors use the terms synonymously, while others restrict the former to tumors composed of large polyhedral or cylindrical cells arranged in tubules or alveoli, and the latter to thin-walled spaces lined by flat or plump endothelial space with the intervening tissue composed of solid masses of similar cells. They occur at all ages but are most common in the second and third decades of life and have no predilection for either sex. The lesions

gross changes are less apparent and the bone shows merely demineralization and thinning of the cortex with little recognizable tumefaction. *Histologically*, the plasma cell variety is composed of typical plasma cells (Fig 401). They are round or somewhat irregular, oval, of moderate sizes, and uniform in appearance. They have a moderate amount of dense cytoplasm, and a single or sometimes double round, eccentric or overhanging nucleus. Its chromatin is evenly distributed and sometimes presents the so-called cartwheel appearance. The cells, as a rule, form large sheets, the degree of vascularity varies, and necrosis sometimes is marked. An associated and interesting lesion is often found in the kidneys. It consists of hyaline casts with peripheral foreign body giant cells plugging the tubular lumens. *Spread of solitary lesions* to other bones, albeit sometimes after five or six years, is generally the rule, while metastases to the spleen, liver, lymph nodes and other organs is not common. In some cases, the reverse is true, that is, the lesions start in extramedullary organs such as the air passages, conjunctiva, lymph nodes, etc., and after as many as ten years become generalized.

The *diagnosis* of myeloma is, as a rule, made from roentgenograms. Sometimes, however, these are essentially normal or they may be confused with senile osteoporosis or metastatic carcinoma from the prostate. For confirmation, therefore, a sternal puncture or biopsy is mandatory. *Treatment* of solitary lesions has been excision, amputation, curettage and irradiation. That of multiple lesions has been symptomatic and most unsatisfactory. The *outcome* is invariably fatal. The average duration of life in the solitary type is about seven years, whereas in the multiple variety, it is approximately two years.

Ewing's tumor was called diffuse endothelioma and endothelial myeloma by Dr Ewing because he considered it to arise from angio-endothelium. Although its histogenesis is still not settled, it is the consensus that reticulum cells of the marrow are the progenitors. Whether the progeny remain as reticulum cells or whether they differentiate into lymphoblasts is still a moot question. The controversy, as in the case of lymph node tumors, evolves about what constitutes a reticulum cell. My own opinion is that the tumor is a lymphoblastic lympho-sarcoma of bone and that reticulum cell sarcoma is a separate neoplasm. Although the tumor has been described as occurring at all ages, most of the patients are between fifteen and twenty-five years of age. Males are affected twice as frequently as females. *Clinically*, there are pain over the involved bone, local swelling, tenderness, sometimes disturbances in the adjacent joints, slight fever, secondary anemia and leukocytosis. *Roentgenographically*, the lesions always start in the medulla. Usually, the process is purely osteolytic with destruction first of the marrow, then of the cortex and finally permeation of the adjacent soft tissue in the form of a small or large mass (Fig 402A). Less often, the tumor stimulates the invaded osteoblasts to new bone formation. This may occur within the medulla but characteristically, in the long bones, it results in a layer of new bone parallel to

the affected areas, pathological fractures, albuminuria, renal impairment, hyperproteinemia, hypercalcemia, anemia, leukocytosis, increased sedimentation rate and *Bence-Jones protein* in the urine. The latter is a beta globulin that probably arises in myeloma and normal marrow cells and is found in the urine in about 50 per cent of the cases when the lesions are multiple. It is detected by heating a test tube of urine in a water bath. When present, a cloud forms as 40°C. is approached; a precipitate appears at 60°C., and the urine becomes clear as the boiling point is reached. The precipitate and then the cloud reappear upon cooling. Finally, from the clinical standpoint, it ought to be pointed out that some cases of multiple myeloma terminate as a frank plasma cell leukemia wherein a leukocytosis as high as 30,000 per c. mm. of blood and plasma cell count of over 50 per cent have been recorded. *Roentgenograms*

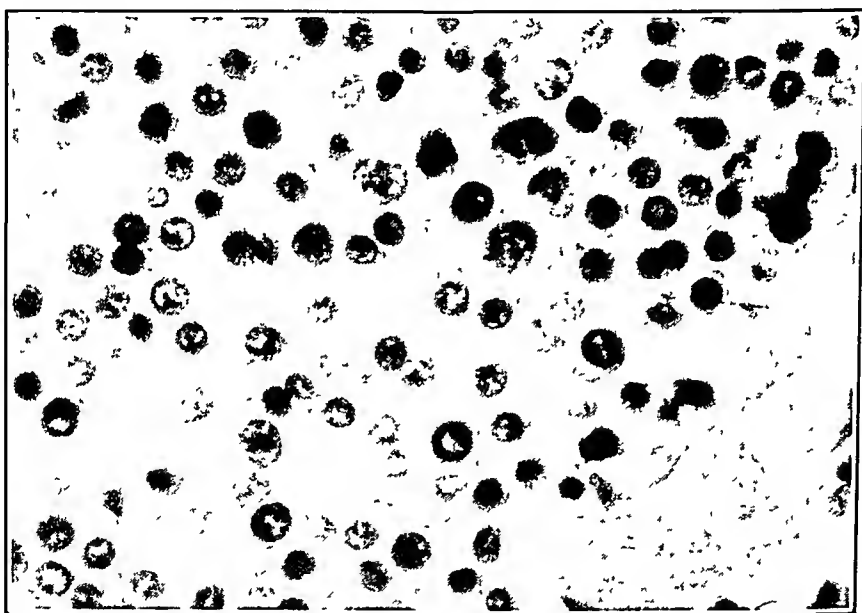


FIG 401 —Multiple myeloma showing numerous plasma cells x 400

usually disclose multiple (occasionally single), discrete, punched out areas of decreased density or osteolysis, with sometimes an extension of the tumors beyond the confines of the periosteum (Fig. 400A). In some cases, however, there may be only a generalized osteoporosis and no tumefactions. The bones most frequently affected are the flat bones of the pelvis, the ribs, sternum, vertebrae and the long bones of the extremities.

Grossly, the lesions are usually multiple but occasionally they are solitary. Externally, the affected bone may be normal; it may show a slight fusiform swelling with the periosteum still intact, or it may show a break through the periosteum with a large infiltrating extra-osseous mass (Fig. 400B). The tumor tissue is usually moderately well demarcated, grey or hemorrhagic, quite soft and contains no intrinsic bone whatsoever. The cortex and adjacent marrow are destroyed and the nodules are single, more confluent or the entire marrow of a given bone is replaced with tumor. At other times, the

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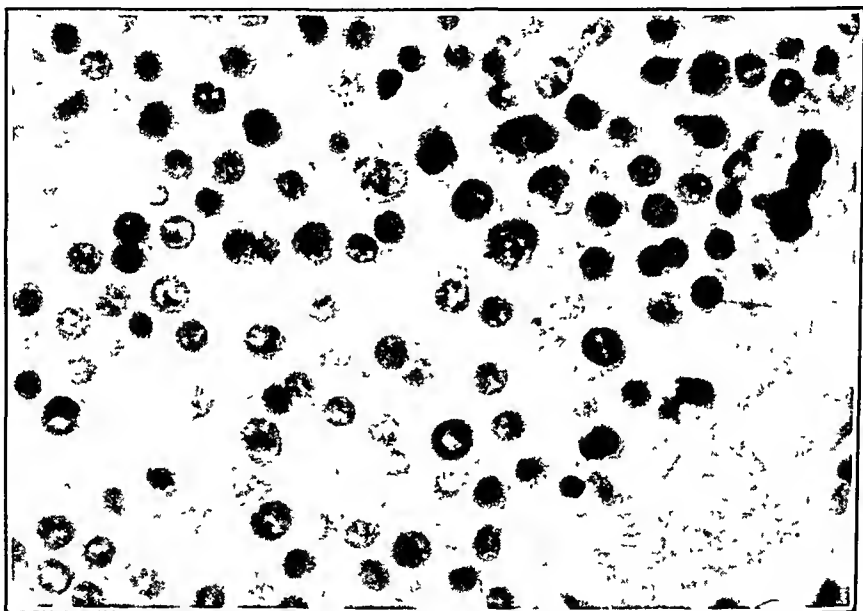


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the cells are often clustered around the vessels to produce a perithelomatous appearance. In areas removed from the vessels where the nutrition is poorer, necrosis is common and when this occurs in small foci, the surrounding viable cells render a rosette-like picture. The cells are by and large round, have ill-defined borders and scanty amount of cytoplasm, and disclose round nuclei that contain finely divided chromatin and frequently nucleoli. Necrosis, nuclear fragmentation, hemorrhage and leukocytic infiltration are not infrequent. Spread of tumor is usually to other bones, although sometimes it is impossible to determine whether this is really a metastasis or whether the tumor is not of multi-centric origin. Aside from bones, the lung and almost all other organs have been known to contain secondary deposits.

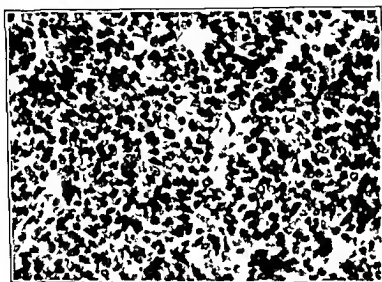


FIG. 403.—Ewing's tumor showing uniform cells with scanty ill defined cytoplasm and round or oval evenly stained nuclei. $\times 200$

The diagnosis is made from the history, roentgenograms and a biopsy. Treatment is irradiation. The tumor readily disappears but the relief is only temporary. Recurrences and new tumors appear within a few weeks or at most months. The prognosis is poor. Most of the patients die within six months.

Lymphoblastomas of bone are less frequent but are otherwise similar to corresponding lesions in lymph nodes. They may be primary in bone or they may reach the bone by direct extension from adjacent nodes by lymphatics or by the blood stream. In infants and young children, the disease is usually present in the form of a leukemia, while in young adults and beyond, it exists as lymphosarcoma, Hodgkin's disease, reticulum cell sarcoma and rarely giant follicular lymphoblastoma. There is no predilection for either sex. Clinically, there are local pain, tenderness and sometimes, tumor. Otherwise, the disease is similar to that when the lymph nodes are primarily involved. Roentgenograms in Hodgkin's disease and in

the old. When the tumor breaks through this layer, it stimulates to the formation of another layer and thus results the so-called onion skin effect. Almost any bone in the body may be involved but the tumor is particularly common in the long bones of the upper and lower extremities, scapula, clavicle, pelvis and ribs.

Grossly, the tumor is usually first apparent as a single mass affecting one bone. Externally, there is a small or large convex protuberance beyond the confines of the bone that is covered by a

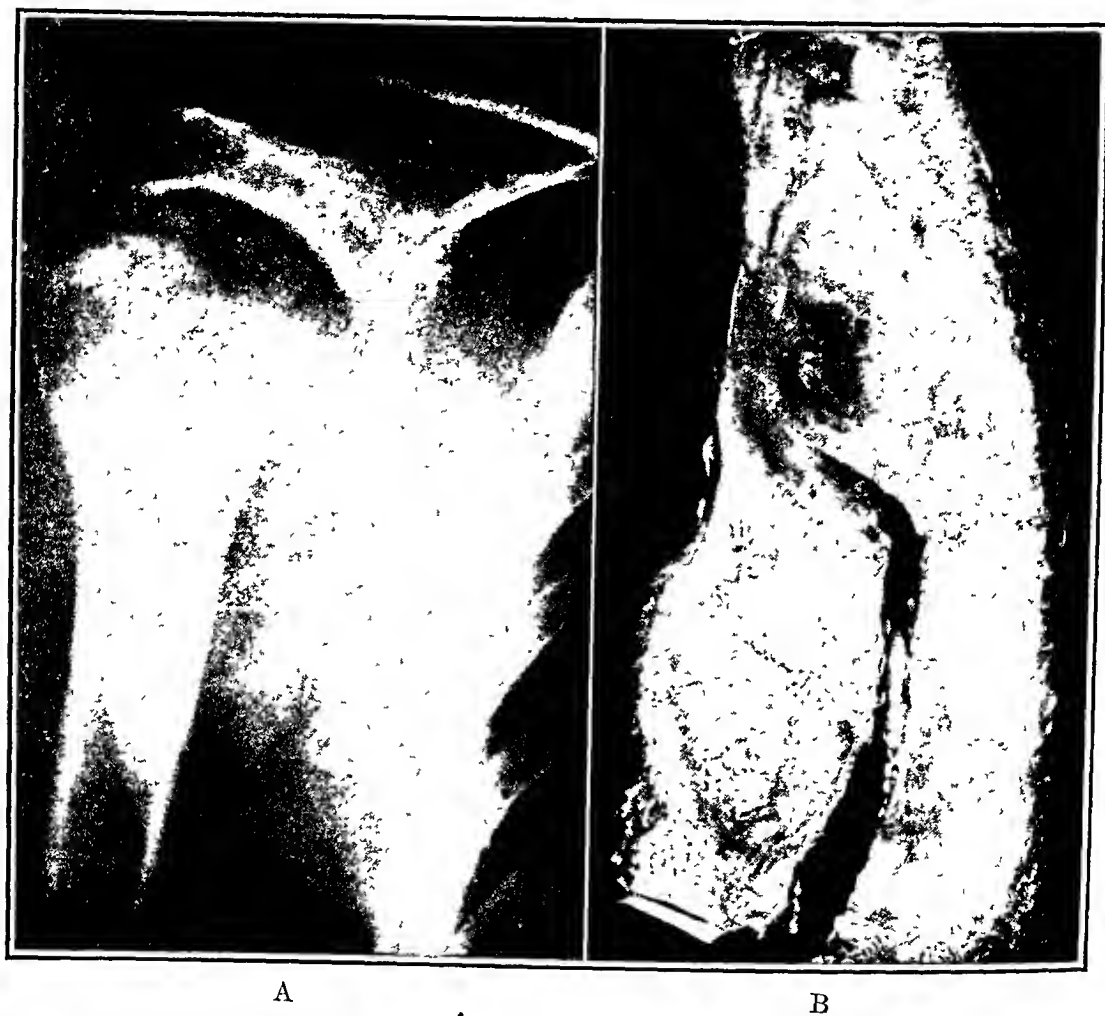


FIG 402.—Ewing's tumor The roentgenogram (A) shows an osteolytic lesion of the scapula. The gross specimen (B) reveals two fusiform swellings of ribs that are still confined by the periosteum.

thin cortex or merely by periosteum and a fibrous tissue capsule (Fig. 402B). The consistency is moderately firm or soft. Cut surfaces reveal homogeneously light grey or hemorrhagic brain-like tissue with frequent areas of necrosis. There is no bone within the tumor itself but about the periphery there may be some reactive osseous tissue. Within the marrow the delineation of the tumor is frequently indistinct so that it is often impossible to tell the extent of the growth. *Histologically*, the cells are monotonously uniform (Fig. 403). They form large sheets that are perforated by moderate numbers of thin walled capillaries. Because of increased nutrition

the cells are often clustered around the vessels to produce a perithelomatous appearance. In are removed from the vessels where the nutrition is poorer, necrosis is common and when this occurs in small foci, the surrounding viable cells render a rosette-like picture. The cells are by and large round, have ill-defined borders and scanty amount of cytoplasm, and disclose round nuclei that contain finely divided chromatin and frequently nucleoli. Necrosis, nuclear fragmentation, hemorrhage and leukocytic infiltration are not infrequent. Spread of tumor is usually to other bones, although sometimes it is impossible to determine whether this is really a metastasis or whether the tumor is not of multi-centric origin. Aside from bones, the lung and almost all other organs have been known to contain secondary deposits.

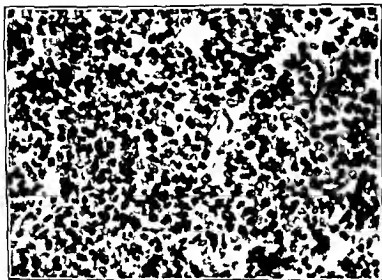


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leukemias (when present in the young) often show some reactive bone formation, but in the others the process is usually osteolytic. Although any bone in the body may be involved, the vertebrae lead the list in frequency. *Pathologically*, the lesions are similar to those found in extramedullary organs and described in the section on the lymph nodes. The *diagnosis* is made from the history, peripheral blood studies, roentgenograms and biopsy. *Treatment* is irradiation. The ultimate *prognosis* is poor.

Liposarcoma originating in bones is rare, there having been less than a dozen cases recorded. The tumor arises in lipoblasts of the marrow. It grows slowly, remains localized for several years before it metastasizes, is osteolytic and pathologically is the same as liposarcoma in extraskeletal tissues. *Treatment* is wide surgical excision, amputation or irradiation. The outcome in the cases recorded has been fatal.

Adamantinoma (adamantinoblastoma) is an uncommon tumor that usually occurs in the tibia, but that has also been described in the femur and ulna. It is found predominately between the second and fourth decades of life and has no predilection for either sex. It is thought to *arise from* misplaced squamous epithelium and histologically duplicates similar tumors that are relatively common in the jaw. The tumor is seen *roentgenologically* as a cystic, osteolytic, cortical defect found anywhere in the diaphysis. *Treatment* has been curettage, resection, amputation and irradiation. Although recurrences are common, metastasis has not yet been described. The ultimate *prognosis* is good.

Metastatic tumors of bone are far more common than are primary neoplasms. The bones most commonly affected are the flat bones (skull, sternum, ribs and pelvis); the vertebrae, and the metaphyses of the long bones. Almost any tumor growing anywhere in the body (except primary tumors of the central nervous system) can secondarily involve the osseous system. In adults, the most common offenders are carcinoma of the prostate, breast, thyroid, kidney and stomach. In infants and young children the tumor is almost exclusively a sympathoblastoma (neuroblastoma). The osseous lesions in cancer of the prostate are most often *osteoblastic* but may be *osteolytic*, while in other tumors the reverse is generally true. Histologically, the secondary growths are usually similar to the parent tissue. The great importance of secondary neoplasms of bone lies in their ability to mimic primary tumors for which the patient may needlessly undergo a mutilating operation. *Sympathoblastomas* particularly, occurring as they do in young patients, may lift and stimulate the periosteum to new bone formation. A roentgenogram of such a growth may be indistinguishable from an osteoblastic osteosarcoma. I have seen one patient who had an entire upper extremity removed for ostensibly an osteosarcoma, only to return several months later with an obvious sympathoblastoma of the retina (Fig. 404).

Mechanical Disturbances.—Mechanical disturbances of bone may be briefly considered under three headings—fracture, vascular occlusions and trauma in relation to neoplasms.

Fractures of bone are common. They may result from trauma to a previous healthy bone or they may occur spontaneously as a result of trivial injury in a previously diseased bone. The latter are called pathologic fractures. Clinically, fractures are classified variously. Our only concern here, however, is to outline the steps in healing. Immediately after the bone has been broken, the defect is filled with blood, debris and leukocytes. Within twenty-four hours, organization in the form of granulation tissue is apparent.

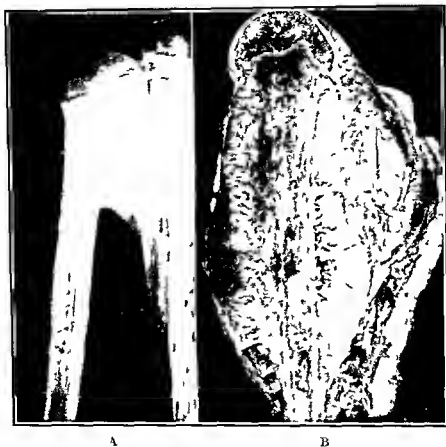


FIG 404—Sympathoblastoma of the retina metastasizing to the right humerus. The roentgenogram (A) and gross specimen (B) are indistinguishable from an osteoblastic osteosarcoma.

This is in turn converted into dense fibrous tissue, fibrocartilage and hyaline cartilage. Concomitantly, osteoblasts from both the periosteum and endosteum near the vicinity of the fracture proliferate, lay down new calcified matrix, and invade and replace the previously deposited fibrous and cartilaginous tissue. In the process of replacement, segments of the latter may be utilized and converted by the osteoblasts into new bone. In approximately three and one half weeks, the defect is bridged by osseous tissue. In cases in which bone grafts have been used, it has been shown that transferred cancellous bone survives and is transformed into cortical

bone, but that cortical bone dies and serves only as a scaffold and a source of calcium.

Vascular occlusions to the bone lead to massive necrosis of the medulla with secondary fibrosis, calcification and cyst formation, if the main nutrient artery is affected or to aseptic necrosis of the epiphysis and articular cartilage, if the blood supply to the end of the bone has been interrupted by a fracture. In addition to vascular occlusion by extreme obliterative endarteritis, *necrosis*, as a result of *irradiation*, is characterized by the death of osteocytes and osteoblasts, absorption and loss of calcium, the presence of osteoclasts and in the mandible (the most common site) the presence of secondary infection.

Trauma as a cause of neoplasms of bone is most difficult to evaluate, but from the standpoint of compensation and liability insurance it is extremely important. There is little doubt that in most instances a single blow or often much more trivial injury merely calls attention to an already present tumor. If this were not so, neoplasms developing after fractures, or the frequently much more severe trauma induced by the orthopedist's chisels and tongs, would be extremely common. They are on the contrary, however, nonexistent. In many courts, the injury is compensable if (1) the trauma is verified and severe enough, (2) if the bone was ostensibly normal before the injury, (3) if the tumor appears at the site of the injury, (4) if the tumor follows the injury by a reasonable length of time and (5) if the diagnosis of tumor is confirmed histologically.

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CHAPTER XXI

JOINTS, TENDONS, BURSAS AND SKELETAL MUSCLES

EMBRYOLOGY AND ANATOMY

Joints are found where bones meet. There are two types—*synarthroses* where little movement occurs and the union consists of connective tissue, cartilage and bone, and *diarthroses* where the joints are freely movable. The latter consist of a joint cavity which appears in the fourth month as clefts in the loose mesenchyme and a capsule which comes from the external tissue that is continuous with the periosteum. The inner surface of the capsule is composed of a flattened layer of cells called the synovial membrane. External to this, there is a layer of fibrous tissue. Some cavities are divided by a fibro-cartilaginous plate called the *articular disc*. *Ligaments* and *tendons* are composed of white fibrous tissue arranged in parallel bundles. As they pass through the joint cavities, they remain covered by synovial membrane. *Bursas* are small spaces in connective tissue over points of friction. Their walls are similar to those of the joints. *Muscle*, both smooth and striated (skeletal), arises from *myoblasts*. In the case of smooth muscle, the latter arise from mesenchyme, whereas, in the case of striated muscle, they arise from myotomes and branchial arches. *Striated muscle* consists of long, tapering cylindrical fibers which may anastomose, end freely within the muscle, or continue uninterrupted throughout the entire length of the muscle. They are composed of a thin covering membrane, the *sarcolemma*, a cytoplasmic mass, the *sarcoplasm*, thin longitudinal cross-striated fibrils called *myofibrils*, and elongated multiple nuclei.

JOINTS

PATHOLOGY

Congenital Anomalies—Developmental malformations of the joints are quite varied. The following more common abnormalities may be listed: (1) *Absence*—associated with absence of bones or portions of extremities. (2) *Dislocations*. The most common is the hip joint and this is due to a shallow shelf of the acetabulum, abnormality in the shape of the head and neck of the femur, an hour-glass contraction of the capsule, long ligamentum teres and delayed ossification of the epiphysis. Two other joints that dislocate are the head of the radius and the knee joint. (3) *Ankylosis* which occurs in single joints such as the elbow or in multiple joints of the extremities when the condition is called *congenital multiple arthrogryposis*. (4) *Club foot*—an adduction, and inversion of the foot. (5) *Congenital flat foot*—the reverse of club foot. In addition, the following acquired deformities of the joints are quite common. (1) *Genu valg-*

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gum—knock knee, (2) *genu varum*—the reverse or bow leg, (3) *Genu recurvatum*—backward curvature of the knee and (4) *hallux valgus*—displacement of the great toe laterally.

Inflammations.—Inflammation of a joint is known as *arthritis*. Strictly speaking, some of the conditions included under this heading are more degenerative than inflammatory, but it is convenient to group them together. Also while some of the lesions are surgical problems, others are not, and the most that a surgical pathologist sees is a biopsy specimen or a portion of a joint. Even at the autopsy table, an entire joint is seldom examined because of limitations of necropsy permits. The genesis, therefore, of some of the lesions, as they occur in man, is still poorly understood. Although classifications of arthritis are rampant and the subvarieties are many, only a few of the more commonly recognized forms will be considered in the following paragraphs.

Acute suppurative arthritis is *caused* by organisms that produce pus. The usual bacteria are staphylococci, streptococci, pneumococci, gonococci, meningococci, influenza bacilli, typhoid bacilli and bacillus pyocyaneus. The organisms *gain entrance* (1) from infections in adjacent tissues, (2) by penetration from the outside and (3) by way of the *blood stream*. The latter is most frequent and often follows debilitating illnesses, exanthemata, or similar infections elsewhere in the body such as pneumonia, septicemia, gonorrhea, otitis media, osteomyelitis, meningitis and tonsillitis. *Clinically*, there are fever, chills, sweats, leukocytosis and locally pain, swelling, redness, tenderness and impairment of movement. The most common *sites* are the knee, hip and shoulder joint. *Pathologic changes* vary greatly from case to case. At one extreme, there may be only a mild congestion, edema and leukocytic infiltration of the synovia, while at the other extreme, there may be extensive destruction of the entire joint. The appearance of the pus varies with the causative organism. Thus when the arthritis is caused by streptococci, it is grey and watery, by staphylococci, thick and creamy, by pneumococci, also thick and grey to green, by pyocyaneus, green and so fourth. *Treatment* consists of antibiotic therapy and chemotherapy, and aspiration or drainage whenever necessary. The *prognosis* depends upon the severity of the infection and the promptness with which treatment has been instituted.

Allergic arthritis is a local reaction in a joint caused by the union of an antigen with an antibody in a sensitive individual. The best example is that seen in serum sickness, that is, in sensitive persons receiving therapeutic injections of animal serum. General reactions such as fever, vomiting, edema of the skin, etc., appear in about a week and a half or two weeks after injection of the serum. Local joint manifestations are present in less than one-fifth of all cases of serum sickness. They consist of exquisite pain, tenderness, swelling and hyperemia. As a rule, they are fleeting and disappear entirely in a few days. Other forms of allergic arthritis are due to sensitivity to drugs, food and bacteria. Among others, the latter is held by some to be the causative agent in rheumatoid arthritis and rheumatic fever.

Traumatic arthritis results from a sudden single injury to a joint or from repeated minor injuries such as incurred by blows, faulty posture and excessive weight bearing. They are common in laborers and in those indulging in sports. A distinction must be made between simple traumatic arthritis, trauma to a joint followed by suppurative or other arthritis and arthritis that is aggravated by trauma. *Clinically*, as a rule, only one joint is affected. There are pain, swelling, and limitations of movement due to muscle spasm. *Pathologically*, there are (1) articular fractures, tears and detachments, (2) hemorrhagic or serous effusion, (3) inflammation and hypertrophy of the synovia, (4) fibrosis of the joint capsule, (5) degeneration of the cartilage and (6) regeneration and excessive production of cartilage and new bone. *Treatment* is aspiration of the fluid and removal of the causative agent.

Tuberculous arthritis is caused by the human or bovine strain of tubercle bacillus. It is almost always secondary to tuberculosis elsewhere in the body, although the visceral lesions may be apparent in only about one-half of the cases. The usual route of infection is hematogenous, but on rare occasions, the joint may be affected by extension from neighboring foci of infection. The disease occurs at all ages, although, in general, involvement of the spine and lower extremities is usually seen in children, while that of the upper extremities is more common in adults. The sites of predilection in approximately decreasing order of frequency are spine (Pott's disease, spinal caries), hip, knee, ankle, sacro-iliac joint, wrist, elbow and shoulder. *Clinically*, general symptoms (consisting of fever, night sweat and loss of weight) may or may not be present. Local manifestations include pain, night cries (from pain due to relaxation of muscles), limitation of movement, swelling, displacement of bones and deformity. *Roentgenograms* early in the disease are normal. Later, the following changes are seen, decreased density of bones adjacent to the joint, focal areas of translucency, widening of the joint space, irregular outline of joint space, increasing destruction of bone, and dislocation.

Pathologically, there is involvement of the synovia, cartilage and bone. The synovia becomes thick, indurated, hyperemic, studded with tubercles and grows both over and under the articulating cartilage. As it does so, the cartilage and subchondral bone are completely destroyed and are extruded into the joint cavity to form a tuberculous or cold (because it is not accompanied by the usual signs of inflammation) abscess. In the process large pieces of cartilage and bone may be detached to form sequestra. In cases that go on to healing, there are ultimately fibrosis, adhesions and ankylosis. *Histologically*, the characteristic changes consist of tuberculous granulation tissue (composed of caseating necrotic material, epithelioid cells, fibroblasts, capillaries and inflammatory cells) admixed with frank tubercles.

The diagnosis of tuberculous arthritis may be difficult in the early stages of the disease especially when visceral manifestations are not apparent. Whenever possible, the clinical diagnosis should be confirmed by biopsy and by recovering tubercle bacilli on culture.

and guinea pig inoculation. *Treatment* is (1) general such as rest, diet, fresh air, sunshine, good food, etc., and (2) local which includes immobilization of joint by traction or fixation, or surgical fusion of the articulating surfaces. The *complications* of a tuberculous abscess are extension, sinus formation, secondary infection and systemic dissemination. The prognosis with regards to restoration of joint function is poor, but with regards to life it is, as a rule, good.

Syphilitic arthritis is rare. In the congenital form, it may arise in conjunction with a syphilitic osteochondritis or it may be similar to the *tertiary* type in *acquired syphilis*. The latter is divided into a non-gummatous and gummatous variety. The *non-gummatous* variety affects the larger joints, such as elbow, shoulder and knee. There are diffuse swelling, pain and effusion of clear or turbid fluid into the joint cavity. The changes are not severe for with treatment there is complete resolution. *Gummatous* arthritis arises as an extension from the synovia or from the bone. The synovia is enlarged, thickened, hyperemic and becomes villous-like. There is a diffuse and perivascular infiltration with lymphocytes and fewer plasma cells, and also an infiltration with small gummas. Extension occurs to the articular cartilage with resulting areas of erosion and massive destruction and less often there is penetration and perforation to the exterior. When the primary focus is in bone, the infection spreads to the joint directly from the diaphysis and epiphysis or by way of the soft tissues. In either case, if prompt treatment is not instituted the entire joint space becomes filled with granulation tissue which in turn is converted into dense fibrous tissue. The articular surfaces are completely destroyed, flattened and adherent and motion becomes restricted or entirely obliterated. On the other hand, if treatment is started before destruction is extensive there is fair regeneration of cartilage and some restoration of movement. In *secondary acquired* syphilis, the arthritis also affects the larger joints and is frequently multiple. The inflammation may be attended by a serous effusion or it may be plastic. With treatment resolution is usually complete.

Charcot's joint is also referred to as a neuropathic joint. Although its pathogenesis is not entirely agreed upon it is probable that the lesion results from repeated trauma to a joint with decreased sensitivity which in turn is caused by an interruption in the reflex arc. While it is true that tabes dorsalis accounts for most of the cases of Charcot's joint, there are also other causes. Some of these are syringomyelia, spina bifida, myelitis, poliomyelitis, toxic neuritis, tuberculosis of the spine, tumors of the cord, and trauma to the spinal cord and posterior nerve roots. The disorder usually appears after the fourth decade of life and affects males in 80 per cent of cases. *Clinically*, the onset is usually insidious but it may be acute. There are effusion, swelling, abnormal mobility, fractures, dislocations, diminished sensory acuity and abnormal function. The sites of predilection are the knee, foot, ankle and hips. *Röntgenograms* disclose destruction, free body formation, demineralization, new bone formation, fractures and dislocations. *Grossly*, these findings are confirmed. Aside from the massive destruction, there

are proliferations of new bone, ossification of the capsule, sclerosis of joint bodies and fragmentation of the articular surfaces and exposed underlying bone. *Histologically*, the synovium proliferates forming a pannus which destroys cartilage, subchondral zone of calcification and subchondral bone. The cartilage undergoes fibrillation, vacuolization and desquamates into the lumen. Simultaneously, the provisional zone of calcification is reactivated and new cartilage is formed from the advancing pannus. Exostoses arise centrally from this newly ossified tissue and also marginally from the periosteum. Meanwhile, the ever present wear and tear in a joint with diminished sensitivity produces more destruction and thus is brought about a vicious cycle. *Treatment* consists of immobilization, arthrodesis or amputation. A serious complication is pyogenic infection. The end result is poor.

Rheumatic arthritis usually occurs in adults and is rarely found in infants or children. It is, of course, one manifestation of rheumatic fever. The joints most frequently affected are the knees, ankles, shoulders and wrists, but any joint may be involved. The lesions are often symmetrical and characteristically, the arthritis is migratory. *Clinically*, the affected joint is swollen, red, hot and extremely tender. *Pathologically*, the postmortem pathologist rarely has the opportunity to examine an acutely inflamed joint in cases of rheumatic fever and a surgical pathologist never sees one. The histologic changes, however, as in the pleura, peritoneum, pericardium and other serosal surfaces are said to reveal Aschoff's nodules. These consist of para-vascular collections of plasma cells, lymphocytes, multinucleated giant cells and fibroblasts all surrounding foci of necrosis. On the other hand, a surgical pathologist does occasionally examine a removed *subcutaneous nodule*. They are characteristically found on the extensor surface of the joints. They are soft, firm or elastic, as a rule painless, appear in crops, last about a week, and measure from a few millimeters to 2 cm. in diameter. They are frequently attached to the tendons, aponeurosis or periosteum. *Histologically*, they are composed of (1) a central area of fibrinoid necrosis, (2) an intermediate zone of edematous connective tissue or epithelioid cells. The long axis of these cells has a tendency to be arranged at right angles to the central mass. The cells are large, sometimes multinucleated and have a basophilic cytoplasm and plump nuclei, and (3) a peripheral zone of edematous connective tissue infiltrated with lymphocytes, plasma cells, monocytes and eosinophils.

Rheumatoid arthritis is also called atrophic arthritis. Its cause is unknown. Although many factors have been incriminated, it is probable that hypersensitivity to bacteria or their toxins may play an etiologic role. Predisposing factors may be dietary deficiencies, trauma and heredity. The disease affects women three times as frequently as men and the most common age is the third and fourth decades of life. The onset may be acute but is usually insidious. The sites of predilection are the small joints of the hand and feet and the involvement tends to be symmetrical. *Clinically*, there are often general symptoms, such as anorexia, fever, fatigue, malaise

and guinea pig inoculation. *Treatment* is (1) general such as rest, diet, fresh air, sunshine, good food, etc., and (2) local which includes immobilization of joint by traction or fixation, or surgical fusion of the articulating surfaces. The *complications* of a tuberculous abscess are extension, sinus formation, secondary infection and systemic dissemination. The prognosis with regards to restoration of joint function is poor, but with regards to life it is, as a rule, good.

Syphilitic arthritis is rare. In the congenital form, it may arise in conjunction with a syphilitic osteochondritis or it may be similar to the *tertiary* type in *acquired syphilis*. The latter is divided into a non-gummatous and gummatous variety. The *non-gummatous* variety affects the larger joints, such as elbow, shoulder and knee. There are diffuse swelling, pain and effusion of clear or turbid fluid into the joint cavity. The changes are not severe for with treatment there is complete resolution. *Gummatous* arthritis arises as an extension from the synovia or from the bone. The synovia is enlarged, thickened, hyperemic and becomes villous-like. There is a diffuse and perivascular infiltration with lymphocytes and fewer plasma cells, and also an infiltration with small gummas. Extension occurs to the articular cartilage with resulting areas of erosion and massive destruction and less often there is penetration and perforation to the exterior. When the primary focus is in bone, the infection spreads to the joint directly from the diaphysis and epiphysis or by way of the soft tissues. In either case, if prompt treatment is not instituted the entire joint space becomes filled with granulation tissue which in turn is converted into dense fibrous tissue. The articular surfaces are completely destroyed, flattened and adherent and motion becomes restricted or entirely obliterated. On the other hand, if treatment is started before destruction is extensive there is fair regeneration of cartilage and some restoration of movement. In *secondary acquired* syphilis, the arthritis also affects the larger joints and is frequently multiple. The inflammation may be attended by a serous effusion or it may be plastic. With treatment resolution is usually complete.

Charcot's joint is also referred to as a neuropathic joint. Although its pathogenesis is not entirely agreed upon it is probable that the lesion results from repeated trauma to a joint with decreased sensitivity which in turn is caused by an interruption in the reflex arc. While it is true that tabes dorsalis accounts for most of the cases of Charcot's joint, there are also other causes. Some of these are syringomyelia, spina bifida, myelitis, poliomyelitis, toxic neuritis, tuberculosis of the spine, tumors of the cord, and trauma to the spinal cord and posterior nerve roots. The disorder usually appears after the fourth decade of life and affects males in 80 per cent of cases. *Clinically*, the onset is usually insidious but it may be acute. There are effusion, swelling, abnormal mobility, fractures, dislocations, diminished sensory acuity and abnormal function. The sites of predilection are the knee, foot, ankle and hips. *Roentgenograms* disclose destruction, free body formation, demineralization, new bone formation, fractures and dislocations. *Grossly*, these findings are confirmed. Aside from the massive destruction, there

equivocal perpendicular arrangement, are more epithelioid and also disclose scattered multinucleated giant cells. The peripheral zone consists of dense fibrous tissue which forms more or less a capsule. Beyond this, the tissue is more vascular and contains scattered monocyctic cells. In *striated muscle* there have been described within the muscle fibers, atrophy, fatty metamorphosis, hydropic degeneration and necrosis. Between the muscle fibers there are collections of plasma cells, lymphocytes and epithelioid cells. Neutrophils or eosinophils are rare or entirely absent. While these muscle changes are most frequently seen in rheumatoid arthritis, they are not specific for they have also been recorded in rheumatic fever and many other debilitating conditions.

The diagnosis of rheumatoid arthritis is not difficult when the disease is typical. *Treatment* is diversified and usually medical. The *prognosis* is guarded for exacerbations are common and one can never be certain that the process is arrested.

Still's Disease—This is probably a form of rheumatoid arthritis, although by some it has been regarded as an entirely independent disorder. It usually starts in childhood but is sometimes seen later. The onset is insidious, or less often acute and the course is chronic. The condition is characterized by multiple and often symmetrical enlargement of the joints and lymph nodes, splenomegaly, anemia, cachexia, muscle atrophy, pericarditis, pleurisy, exophthalmos and exanthemata.

Marie-Strumpell arthritis is regarded by most authors as a form of rheumatoid arthritis that is limited to the sacro-iliac joint and spine. The disease starts in the former joint and gradually ascends to involve most or all of the spine. The initial change is a synovitis accompanied by proliferation of connective tissue. This obliterates the joint space and gradually replaces the cartilage. The fibrous tissue then undergoes calcification and this together with calcification of the ligaments that surround the spine transform the latter into a solid bony column (poker back). *Roentgenograms* readily reveal these changes along with osteoporosis of the vertebrae proper. *Clinically*, the disorder usually starts in the third decade of life, affects males in 90 per cent of the cases, and often follows an injury to the back. Initially, there is intermittent pain over the sacral or lumbar regions which is most severe after several hours rest in bed. As the infection ascends, nerve root pains may become excruciating and, of course, follow the distribution of the affected nerves. Aside from the pain, there are loss of appetite and weight, irritability, fatigability, anemia and an increased sedimentation rate. Spasm of the flexor muscles of the spine reduces normal lumbar curve and often results in severe *kyphosis*. If the position is not corrected before calcification occurs, such deformities become permanent. Eventually after a period of years, the disease "burns itself out" leaving in its wake a rigid spine with or without a faulty posture.

Osteo-arthritis is also known as hypertrophic or degenerative arthritis. It is a disease of older and often overweight people. Among the many listed causes are aging of the cartilage, circulatory disturbances, trauma, faulty constitution of the cartilage, chilling

and loss of weight. Locally, the interphalangeal joints are first affected whence the disease extends towards the trunk. There are pain, stiffness, impairment of motion, exquisite tenderness and fusiform swelling. About one-fifth of all cases exhibit subcutaneous nodules which are similar in distribution and attachment to those seen in rheumatic fever. In contrast, however, the nodules are larger, more numerous, more definite in outline and often persist for years. *Roentgenograms* disclose initially soft tissue swelling and osteoporosis, while later they disclose decrease of joint space, punched out areas at bone margins and osteophytes.

Pathologically, the changes may be considered under joints, subcutaneous nodules and muscles. The initial changes in the *joints* are seen in the synovia. It becomes thickened, edematous, hyperemic and hemorrhagic and sends a pannus over the articular cartilage.



FIG 405 —Rheumatoid arthritis showing an articular surface of the knee joint covered with dense fibrous tissue

As a result, the nuclei of the cartilage shrink, become granular and disappear and the remaining matrix now staining eosinophilic is gradually absorbed. Concomitantly, the central portion of the articular cartilage discloses a blister-like area into which grow blood vessels from the subchondral bone marrow. The effect of these is to produce vacuolization and disappearance of more cartilage cells and destruction of subchondral bone. Although there is some attempt at new cartilage and bone formation, most of the replacing granulations are converted into dense fibrous tissue. This along with villous ingrowths from the synovia result in intra-articular adhesions and ankylosis (Fig. 405). The *subcutaneous nodules* are quite characteristic. They consist of the same three layers already described in connection with the rheumatic nodules. The central area of necrosis is, however, more complete and discloses softening, liquefaction and deposition of cholesterol and fatty crystals. The intermediate zone is more conspicuous. Its cells possess an un-

the time of an acute attack. *Histologically*, they are composed of a central area of necrosis containing the crystals and an outer layer of granulation and fibrous tissue. Within and about the latter the vessels frequently disclose an arteritis. In the necrotic area, there may or may not be foreign body giant cells and secondary deposits of cholesterol or calcium. When deposited in the periarticular tissues, the urates usually bring about fibrosis, contractures and limitations of movement, whereas within the joint, they excite the formation of a pannus which later results in true ankylosis. *Treatment* is dietary consisting essentially of a low purine diet. The *prognosis* with regards to life is good, but with regards to morbidity it is poor. Eventually *death* usually results from renal or cardiovascular complications.

Hemophilic arthritis is caused by hemorrhage into a joint in a patient with hemophilia. The blood accumulates under pressure and through the medium of broken down pigments causes hypertrophy, hyperplasia and fibrosis of the synovia and periarticular tissues. As a result, the adjoining margins of articular cartilage become first eroded and then stimulated to produce osteophytes. Hemorrhages within the subchondral bone result in cavitations that can be seen roentgenographically. When these reach the articulating cartilage, the latter too is destroyed. The final result is ankylosis. The joints affected in order of frequency are knee, ankle, elbow, hip, fingers, wrist, spine and toes. *Clinically*, acute involvements practically always start in childhood and consist of rapid effusion, pain and disability. After one or more attacks the joint remains tender and swollen and the muscles atrophy. *Treatment* is that for hemophilia in general, avoidance of trauma, aspiration of the blood if pain is intense, support by bandages when the disease is chronic and correction of severe deformities. The disorder is characterized by remissions and exacerbations.

Hypertrophic pulmonary osteoarthropathy is an enlargement of the terminal phalanges of the fingers due to hypertrophy and hyperplasia of the surrounding soft tissues and synovia and to deposition of new bone by the periosteum. The process results from over-nutrition of the parts as a result of increased vascularity, but the cause of the latter is unknown. The disorder accompanies a host of chronic pulmonary, pleural and mediastinal diseases and less often cardiac, hepatic and gastrointestinal lesions. It occurs at any age, has a sex distribution of the accompanying disease, is, as a rule, symptomless and in addition to the phalangeal enlargement, discloses a lateral and longitudinal convex deformity of the finger nail.

Heberden's nodes are small protrusions in the vicinity of joints most commonly associated with osteo-arthritis, but also seen in conjunction with rheumatoid arthritis, tuberculosis of bones, ochronosis and other disorders. The protrusions arise insidiously, are found on the lateral aspects of the terminal joints, are rarely larger than 6 mm. in diameter, are firm, soft or cystic and pathologically consist of true bony exostoses or soft tissue proliferations.

Tumors—Neoplasms of the joints are uncommon. The following have been described from fat, a lipoma, from blood vessels,

and dampness. The site of predilection is usually a larger joint, such as the knee, hip, shoulder, sacro-iliac and vertebrae or the smaller terminal joints of the fingers. *Symptoms* and *signs* arise insidiously and consist of stiffness of the joint, pain on motion, swelling due principally to effusion and later, when the cartilages are destroyed, a sensation of grating upon movement. *Roentgenograms* in the fully developed case disclose lipping and exostosis of the articular margin, destruction of the articular surface and narrowing of the joint space.

Pathologically, the process consists of patchy areas of degeneration, softening and denudation of the articular cartilage with at first intervening areas of normal cartilage remaining. Eventually, even these soften and disappear leaving only the bare underlying bone which by friction becomes polished or eburnated. At the periphery of the joint, the perichondrium is stimulated to produce first cartilage and then bone which grows outward to produce the well-known lipping. The synovia is usually undisturbed but in advanced cases it may form villous projections into the lumen. Heberden's nodes (see below) are said to be common in osteo-arthritis.

The *diagnosis* is established from a history of a slowly progressive, monarticular lesion occurring in older people together with characteristic changes roentgenographically. *Treatment* among other things consists of protection to the joint, irradiation therapy and various forms of surgery. It must be emphasized that more often than not such joints are asymptomatic and require no therapy. Ankylosis of any great degree seldom occurs. The *prognosis* is, therefore, much better than in most other forms of arthritis.

Osteochondritis dissecans is a disease of young, predominately male adults that usually affects the knee joint. Its *causes* are listed as hereditary, direct trauma, subchondral fractures, pull of ligaments, vascular occlusion and embolism. *Symptoms* and *signs* consist of pain, weakness in the joint, dysfunction, tenderness and effusion. *Pathologically*, the articular hyaline cartilage changes to fibro-cartilage. This becomes deeply furrowed and separated off in the form of small fragments that escape into the cavity where they form "joint mice." The latter can usually be seen radiographically. If symptoms are marked enough, treatment is surgical removal of the loose bodies.

Gout is a hereditary, metabolic disease of unknown etiology that predominates in males and is characterized by an elevated uric acid level in the blood, tophi and acute attacks of arthritis. The latter appear suddenly and without warning, are attended by severe throbbing pain and are most often found in the great toe. The arthritis lasts a few days or weeks, completely disappears and then returns in about a year or so. Subsequent attacks are more severe and closer together. Their duration may be considerably shortened by the ingestion of colchicine. *Gouty tophi* are deposits of monosodium urate in various tissues of the body but most commonly in the helix of the ear and in periarticular structures. They vary in size from less than 1 mm. to about 10 mm. in diameter, are sharply circumscribed, white creamy or yellow, and are painless except at

bodies arising within the joint, many exogenous objects can be introduced into the cavity

Contusions and Sprains—A *contusion* is a bruise resulting from a direct blow and consisting of a disruption of smaller tissues and vessels. If the vessels are larger and more blood escapes, a *hematoma* will form. Clinically, there are pain, swelling, tenderness and inability to use the joint. If the skin is abraded, secondary infection is common. A *sprain* consists of a wrenching of a joint with tearing of the capsule, ligaments, or synovial membranes. It is due to an indirect force and is often accompanied by tearing of fragments of bone or cartilage and by fractures. The most common site is the ankle joint. A sprain is always accompanied by a contusion. If the force is severe enough and if the damage to the periarticular



FIG. 406.—Baker's cyst. The wall is thick and fibrous. The inner surface is smooth. The lumen contains a loose cartilaginous body.

structures is of sufficient magnitude, there is also an associated *dislocation*.

Baker's cyst is either a herniation of the synovia through the posterior part of the capsule of the knee joint or an escape of fluid from the joint proper into the adjoining bursas through communicating ostia. Motion favors the escape of fluid and, thereby, the enlargement of the cyst. *Symptoms* consist of aching and stiffness of the knee and a painless tumefaction. The condition has no predilection for either sex, affects one side as often as the other and occurs at all ages. *Grossly*, the communication with the cavity of the knee is, as a rule, narrow. The sac usually measures less than 10 cm. in diameter but it may be much larger, is composed of dense firm grey tissue, has a smooth lining, is unilocular or multilocular, and is filled with mucinous, clear or straw-colored fluid (Fig. 406). It may contain loose bodies. *Histologically*, the lining is composed of

a hemangioma; from cartilage, a chondroma, and from synovia, a giant cell tumor and a synovioma. The former need no further elucidation since they have been adequately covered in the sections on the skin and bone. Giant cell tumor is considered subsequently under tendons. Synovioma alone merits further discussion.

Synovioma as the name implies is a tumor that originates in synovia and, as such, is found not only in joints but also in connection with tendons and bursas. The *synonyms* are synovial sarcoma, synovial sarcoendothelioma and cancerous synovial tumor. The most frequent locations are the knee joint and thigh but they have also been described in the buttocks, leg, foot, toes, axilla, elbow, forearm, wrist, hand and fingers. They affect males one and a half times as frequently as females and occur at all ages but are most common around the thirtieth year. *Clinically*, the most outstanding symptom is pain which may precede the formation of a detectable tumor by even years.

Grossly, the growth is fairly well-circumscribed but not encapsulated, varies in size but is generally small, and is closely attached to the adjacent joint capsules, tendons and muscles. The external surface is usually bossed or nodular, and the consistency is firm, soft or hard. Cut surfaces disclose light grey tissue with scattered areas of necrosis that appear yellow, areas of old and recent hemorrhage that appear brown and red, and foci of calcification that appear as small gritty particles. The tumors do not project into the joint cavity. *Histologically*, both the normal components of the synovia are present in varying proportions. The fibromatous element appears as an ordinary fibrosarcoma. The cells are spindle-shaped, ill-defined and contain an abundant or scanty amount of cytoplasm. The nuclei are plump, spindle or oval, and deeply basophilic. The synovial cells are spindle-shaped and arranged in cords or sheets or they are cuboidal and columnar and line slit-like spaces. The latter are prone to exhibit papillary or tuft-like projections into the lumens. Synovial cells can frequently be identified by the presence of mucicarmine positive droplets within their cytoplasm. The tumors may remain localized for years, but eventually they metastasize by the blood and lymph vessels to the lungs, skin, bones and lymph nodes.

The *diagnosis* is usually made only by biopsy. *Treatment* of choice is amputation of the extremity when the tumor is favorably located, otherwise it consists of wide local excision. The ultimate *prognosis* in the recorded cases has been poor. The duration of life varied from five months to sixteen years.

Mechanical Disturbances.—Under this heading joint mice, contusions and sprains, and Baker's cyst may be briefly considered.

Joint mice are loose bodies within a joint cavity that arise from the adjacent tissues (Fig. 406). They may be fibrinous, fibrous, fatty, cartilaginous, osseous and mixtures of all of these. They arise in conjunction with the following conditions: (1) Arthritis, such as arthritis deformans, Charcot's joint, osteochondritis dissecans, osteoarthritis, syphilis, tuberculosis, non-specific chronic infection and gout. (2) Neoplasms, such as chondromata. (3) Mechanical disturbances, such as hemorrhage and fracture. In addition to foreign

and contains milky white fluid, caseous cheesy material, or dry amorphous partly calcified granules. The adjoining fibers of the tendon are dull and stringy. *Histologically*, the tendon initially loses its wavy appearance and becomes granular, clear, homogeneous and fibrillated. Foci of degeneration then become apparent and the vascularity increases. Foci of calcification are deposited in the areas of degeneration and foreign body giant cells may make their appearance. The adjacent synovia shows villous formations, increased vascularity and proliferation of the connective tissue and lining cells.

The *diagnosis* is usually made from the history, physical examination and roentgenograms. *Treatment* of choice is operative incision with removal of the deposits or excision of the diseased tissues. The *results* are good.

Tuberculosis of tendons and bursas usually results from an extension of an infection from an adjacent focus which is, as a rule, a joint or a bone. Rarely, the trochanteric and pretibial bursas are involved separately.

Syphilitic tenosynovitis and *bursitis* are probably more common than recognized. Acute and subacute *tenosynovitis* have been described in secondary syphilis, but these are usually as evanescent as are the other manifestations in this stage. In the tertiary stage, painless nodules composed of milium or larger gummas are found along the course of the tendons. There is also an associated plastic exudation, thickening and infiltration. The lesions are more common in the larger tendons, such as biceps, achilles, triceps and extensor muscles of the fingers. Clinically, there may be a positive history of syphilis, other stigmata of the disease and as a rule, a positive blood Wassermann. The lesions disappear under specific therapy. *Syphilitic bursitis* is also seen in both the secondary and tertiary stages of the disease. There is frequently little associated pain but unless specifically treated the lesions persist. The changes are both proliferative and degenerative resulting in a filling of the lumen of the sac with a viscid yellow fluid. The bursas, are as a rule, inadvertently removed.

Tumors—Neoplasms of tendons and bursas are similar to those of joints. There have been described the following benign growths, ganglion, giant cell tumor, lipoma, hemangioma, lymphangioma, fibroma and chondroma and the following malignant tumors, synovoma, fibrosarcoma and chondrosarcoma. Only two of these, namely, ganglion and benign giant cell tumor need to be considered further.

Ganglion—This is a cystic swelling that arises in and is attached to a tendon sheath or capsule of a joint. The most frequent locations are the dorsum of the wrist, dorsum of the foot, ankle, knee, popliteal region and volar aspect of the fingers. The lesion is more common in females and, although it may occur at all ages, it is prevalent in the second, third and fourth decades of life. The most frequent *symptom* is the swelling. In one-half of the cases, there are, in addition, pain and impairment of function. *Grossly*, the lesion is smooth, rounded, tense, cystic and measures as much as

synovial cells. Beneath this, there is frequently an infiltration with lymphocytes, while externally, there is a layer of fibrous tissue. The latter may contain moderate numbers of blood vessels, cartilage and hemosiderin. *Treatment* of choice is excision. The *prognosis* is good.

TENDONS AND BURSAS

PATHOLOGY

Inflammations.—Inflammatory lesions of the tendons and bursas may be divided into acute non-specific, chronic non-specific, tuberculous and syphilitic.

Acute non-specific tenosynovitis and bursitis may be *caused* by (1) a single or repeated *trauma*, such as kneeling or the rub of a shoe. In these cases, there is thickening of the capsule and roughening of the inner surface so that upon movement grating is heard and felt. Later, there is usually an associated effusion, and (2) *bacteria*. The latter is much more serious. It results from direct inoculation of the organisms from without, from extension from nearby foci of infection and, rarely, from blood stream metastasis. The most common organisms are the staphylococci and the streptococci and, rarely, blood borne bacteria such as the gonococci. Suppurative infections are common in the hands. The organisms usually gain entrance by way of puncture wounds of the transverse creases of the fingers. The infection rapidly spreads to involve the entire sheath, and this, in the case of the thumb and little finger, means extension to the wrist. *Locally*, there are swelling, pain and exquisite tenderness, while generally there may be fever, chills and malaise. *Pathologically*, the changes are those of any acute suppurative infection. *Complications* consist of sloughing of the tendon, arthritis, osteomyelitis, adhesions and ankylosis. *Treatment* consists of antibiotic therapy and chemotherapy, and adequate drainage. *Good results* are obtained in less than two-thirds of the cases.

Chronic non-specific tenosynovitis and bursitis is by far most common in the shoulder joint and is responsible for the so-called "painful shoulder." The *synonyms* are calcification of the shoulder cuff, subdeltoid bursitis, calcified subacromial or subdeltoid bursitis and peri arthritis. The precise *cause* of the condition is not known, but it is thought that faulty nutrition causes degeneration of the supraspinatous tendon and that subsequent changes result from wear and tear, friction, direct trauma and by constant abduction of the arm. *Symptoms* are usually absent until some form of trauma is sustained when there is sudden and severe pain with disability. *Roentgenograms* show calcification between the humeral head and the acromion.

Grossly, the bursa is thick, edematous and vascular. It may contain calcareous deposits but is usually empty. Its floor (that over-rides the supraspinatous tendon) may be covered with tiny villi and contains an elevated somewhat softer bulge. The latter represents nothing more than a cystic degeneration of the tendon

hereditary background. The disorder is about fifteen times more common in males than in females, usually appears after forty years of age, and may be unilateral or bilateral. The first manifestations consist of small indurations or nodular thickening of the palms with puckering of the overlying skin. Within a few months or many years, there is noted increasing contraction of the fascia that extends from the palm to the first inter-phalangeal joint. Extension of the affected finger increases the prominence of the band and is frequently attended by pain. *Histologically*, there are hyperkeratosis of the epidermis, disappearance of the papillae, fibrosis of the corium, lymphocytic infiltration of the corium, depletion of the subcutaneous fat and a hypertrophy and hyperplasia of the palmar fibrous tissues. The latter consists of parallel or interlacing bundles of cellular or hyalinized fibrous tissue with plump nuclei and scanty

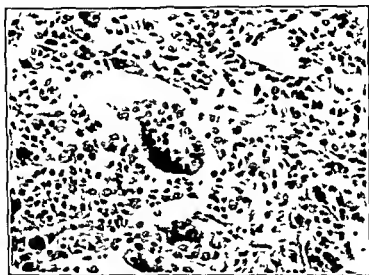


FIG 408.—Benign giant cell tumor of tendon sheath origin disclosing polyhedral spindle and foreign body giant cell. $\times 100$

or abundant amount of eosinophilic cytoplasm. Treatment is fasciotomy or excision of the contracting bands. The latter offers the only permanent relief.

Rupture of the tendons occurs (1) from laceration in an open wound. Many tendons may be injured in this manner and the injury consists of partial or complete severance. In the latter, the tendons retract and are difficult to find. The greatest surgical problem is to prevent or combat infection, and (2) from indirect violence or non-penetrating trauma. These result from contusions, sprains, falls, violent exercise or direct blows. The tendon may be partially or completely torn or it may be detached from its point of insertion into the bone. There are intense pain, local tenderness, presence of a gap to palpation and loss of function. The tendons most commonly affected are Achilles, plantaris, extensor quadriceps, supraspinatus, long head of the biceps, extensor communis digitorum, and extensor pollicis longus.

3 cm. in diameter. Cut surfaces disclose a unilocular or multilocular cavity with fibrous walls, smooth inner surfaces and containing clear, stringy, mucoid material (Fig. 407). *Histologically*, the wall is composed of dense collagenous connective tissue which may or may not be lined with synovial cells. In young cysts, one may encounter spheroidal cells that are being distended with mucoid material. When the cell boundaries break the latter is liberated and accumulates to form the cyst contents. One-half of the cysts disappear spontaneously. *Treatment* in the rest is aspiration of the contents or excision of the entire lesion.

Giant Cell Tumors.—These arise in connection with tendon sheaths and aponeuroses. They have *also* been called xanthomatous giant cell tumor, giant cell sarcoma, xanthosarcoma and myeloma. The most common location is the fingers at the interphalangeal or metacarpophalangeal joints. Other sites are the sesmoid bones, palms, wrists, toes, ankles, arms and legs. The only symptom they produce is a swelling that measures to as much as 4 cm. in diameter.



FIG. 407.—Ganglion showing an irregular, smooth-walled, unilocular cavity. The contents have been evacuated.

Grossly, the tumor is encapsulated, lobulated and firm and its cut surfaces are homogeneously yellow or yellowish-brown. *Histologically*, it is composed of varying proportions of (1) polyhedral or spindle cells with a moderate amount of eosinophilic cytoplasm, (2) large giant cells of the foreign body type, (3) well-defined polyhedral foam cells with granular cytoplasm, (4) deposits of hemosiderin and (5) the occasional presence of fibrocartilage and bone (Fig. 408). *Treatment* is complete surgical excision. A malignant transformation is extremely rare and even then the tumor remains localized. The *prognosis* is, therefore, good.

Mechanical Disturbances.—These consist of Dupuytren's contracture and rupture of the tendons.

Dupuytren's contracture is a proliferative and contracting lesion of the palmar fibrous tissues, the chief structure of which is the palmar fascia. The precise *cause* of the condition is not known, but of the many theories suggested, it appears that the most likely factors are trauma in a person with a "fibroblastic diathesis" and a

hereditary background. The disorder is about fifteen times more common in males than in females, usually appears after forty years of age and may be unilateral or bilateral. The first manifestations consist of small indurations or nodular thickening of the palms with puckering of the overlying skin. Within a few months or many years, there is noted increasing contraction of the fascia that extends from the palm to the first inter-phalangeal joint. Extension of the affected finger increases the prominence of the band and is frequently attended by pain. *Histologically*, there are hyperkeratosis of the epidermis, disappearance of the papillae, fibrosis of the corium, lymphocytic infiltration of the corium, depletion of the subcutaneous fat and a hypertrophy and hyperplasia of the palmar fibrous tissues. The latter consists of parallel or interlacing bundles of cellular or hyalinized fibrous tissue with plump nuclei and scanty

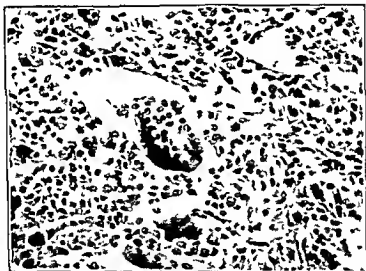


FIG. 408.—Benign giant cell tumor of tendon sheath origin disclosing polyhedral spindle and foreign body giant cells. $\times 100$

or abundant amount of eosinophilic cytoplasm. *Treatment* is fasciotomy or excision of the contracting bands. The latter offers the only permanent relief.

Rupture of the tendons occurs (1) from *laceration* in an open wound. Many tendons may be injured in this manner and the injury consists of partial or complete severance. In the latter, the tendons retract and are difficult to find. The greatest surgical problem is to prevent or combat infection, and (2) from *indirect violence* or *non-penetrating trauma*. These result from contusions, sprains, falls, violent exercise or direct blows. The tendon may be partially or completely torn or it may be detached from its point of insertion into the bone. There are intense pain, local tenderness, presence of a gap to palpation and loss of function. The tendons most commonly affected are achilles, plantaris, extensor quadriceps, supra-pinatus, long head of the biceps, extensor communis digitorum, and extensor pollicis longus.

SKELETAL MUSCLES

PATHOLOGY

Congenital Anomalies.—Three developmental abnormalities will be considered here, namely, scalenus anticus syndrome, amyotonia congenita and progressive muscular dystrophy.

Scalenus anticus syndrome is identical with that produced by a cervical rib or anomalies of the first rib. *Clinically*, it consists of (1) remissions and exacerbations of acute lancinating or dull aching pain that is distributed down the arm, around the shoulder, to the scapula, to the occiput or is confined to the cervical region, (2) atrophy, twitching and weakness of the intrinsic muscles of the hand, (3) vasospasm with reduction of temperature in the fingers and (4) partial occlusion of the lumen of the subclavian artery with reduction in amplitude of the pulse and in the blood pressure. The *scalenus anticus* is a stout *muscle* that arises from the anterior tubercles of the transverse processes of the third, fourth, fifth and sixth cervical vertebrae, and after a vertical course is inserted into the scalene tubercle on the inner border of the first rib and into a ridge of the first rib in front of the subclavian artery. The brachial plexus passes between the middle and anterior scalene muscles and then over the first rib and behind the clavicle. The *cause* of the syndrome is not definitely known, but it is thought that direct or indirect trauma to the scalenus anticus produces spasm which results in elevation of the first rib. This compresses the brachial plexus and subclavian artery bringing about more spasm and, thereby, producing a vicious cycle. Other theories are pressure by an overdeveloped scalene muscle, relaxation of musculature and sagging of the shoulder girdle, descent of the shoulder but lack of descent of the sternal end of the clavicle, and abnormal development of the brachial plexus wherein a portion arises within the thorax. The syndrome is most common in the third decade of life and predominates slightly in females. *Treatment* is conservative or consists of surgical severance of the scalenus anticus. The condition must be differentiated from the much more serious tumor of the thoracic inlet producing the Pancoast syndrome (see Chapter V, p. 201).

Amyotonia congenita is a hereditary and sometimes familial weakness of the striated muscles. When mild, it interferes with normal posture, but when more severe, the patient can neither walk nor sit up. Death usually results from pneumonia due to failure of the muscles of respiration. *Grossly*, the muscles are pale, small and flabby. *Histologically*, they are embryonic in type, small or of normal size, disclose an increase of the nuclei of the sarcolemma but do not show any degeneration. There is an increase of fat and connective tissue between the muscle fibers. The central nervous system in some cases is normal, but in others it shows a reduction in the number of cells in the anterior horns of the spinal cord and demyelination of the anterior nerve roots.

Progressive muscular dystrophy is a hereditary and familial degeneration and atrophy of striated muscles. The disorder usually

starts, in childhood after an infectious disease, trauma or over-exertion, and it affects males seven times as frequently as females. Initially, the muscles of the thigh and calf are involved, but later, other muscles such as the gluteus, supraspinatus, infraspinatus and tongue are also affected. *Symptoms*, early in the disease, consist of pain which may be severe enough to prevent sleep, while later, there are weakness of the involved muscles, winging of the scapulas and a lumbar lordosis. *Grossly*, the muscles appear pale and are usually larger than normal. *Histologically*, the muscle fibers are reduced in size and show varying stages of degeneration. Some are pale, others are darkly stained. The cytoplasm shows fibrillation, hyalinization, granulation, vacuolization and disintegration. Within these fibers, there appear groups of deeply stained nuclei that are thought to represent phagocytic cells and are called myophages. Throughout areas of degeneration, unaffected muscle fibers are hypertrophied, thickened and disclose an accentuation of their cross striations. As the muscle fibers and bundles disappear, they are replaced with fat and connective tissue which account for the bulkiness of the muscle despite its loss of quality. Although numerous drugs have been tried, *treatment* or progressive muscular dystrophy remains entirely ineffective.

Inflammations—Under this heading may be considered the following: suppurative myositis, polymyositis, dermatomyositis, myositis ossificans, trichinosis, periarteritis nodosa and temporal arteritis.

Suppurative myositis usually arises as an extension of a pyogenic infection in the skin or subcutaneous tissues. Some of the more common primary inflammations are furuncle, carbuncle, cellulitis, infected lacerations and trophic or decubitus ulcers. Less commonly the organisms are blood borne and have followed such distant infections as gonorrhea and typhoid fever. The local *manifestations* are those of any acute infection, namely, swelling, pain, tenderness and, if the process is superficial enough, heat and redness. *Grossly*, there may be a brawny induration or the entire area may be soaked in pus. *Histologically*, there are congestion, edema, leukocytic infiltration, degeneration and necrosis of muscle and other tissue, and proliferation of fibrous tissue.

Polymyositis is an acute infection caused by a virus which produces destruction of the anterior horn cells of the spinal cord and brings about paralysis of groups of striated muscles. *Grossly*, the muscles are pale and flabby. *Histologically*, there are the following: (1) Atrophy of muscle fibers. This is evidenced by a decrease in size, granularity of the cytoplasm, an apparent increase in number of nuclei and a complete disintegration of other fibers with only granular debris remaining. (2) Hypertrophied fibers scattered among the degeneration and dead fibers. (3) A substitution of fibrous and fat tissue.

Dermatomyositis is an acute or chronic disease of unknown etiology that affects both the skin and the muscles. It has no predilection for either sex and is most common in the second, third and fourth decades of life. *Clinically*, the onset is acute with fever,

malaise and anorexia, or it is more insidious. The skin is edematous, dry, scaly, hyperesthetic and pigmented. The muscles of the extremity or trunk are swollen, painful and tender. As the acute manifestations subside, there are left palpable and indurated areas that are followed by contractures. Death is brought about by affliction of the muscles of deglutition and respiration. *Histologically*, the skin discloses atrophy of the epidermis, disappearance of the rete pegs, vacuolization of the basal layer of cells, flattening of the papillae, fibrosis and edema of the dermis and lymphocytic infiltration about the vessels, sweat glands and hair follicles. The muscles reveal edema and later fibrosis of the supporting connective tissue, perivascular infiltration with lymphocytes, and degeneration and disappearance of the muscle bundles. *Treatment* of the disorder is most disappointing for nothing known today will stop the progress of the disease. The *prognosis*, therefore, is grave. The immediate death rate is more than 50 per cent, and because of atrophy and fibrosis most of the survivors ultimately become chronic invalids.

Myositis ossificans is, as a rule, divided into two types—localized and progressive. The *localized* form is also known as traumatic ossifying myositis, ossifying hematoma and calcified hematoma. As the name suggests, the condition usually follows trauma and can occur as early as ten days after injury. The most common sites are above the elbow and in the thigh. The origin of the osseous tissue is thought to be from implants of periosteum in the muscle, from ossification of a hematoma or from metaplasia of connective tissue. Roentgenologically, the lesions are seen as streaks that follow the muscle fibers or as irregular blocks of opaque material radiating from the periosteum. The *progressive* form is familial and hereditary. It consists of deposition of calcium and bone in muscles, tendons, ligaments, fascias and aponeuroses. It affects males four times as frequently as females and is often associated with a small big toe that discloses ankylosis of its proximal phalangeal joint. Clinically, the disorder starts in any location, following trauma or infection, as a small cyst-like mass that breaks down, drains and calcifies, or it starts as a generalized rheumatic type of infection with subsequent development of masses in the muscles. The muscles of the back are particularly prone to involvement and with progression of the lesions are converted into a solid mass of bone. *Histologically*, the transformation apparently takes place first in the connective tissue and the muscles are then replaced by a process of atrophy and degeneration. The *diagnosis* is made roentgenographically. *Treatment* is unsatisfactory. The *prognosis* is poor for, if the disease starts in early childhood, death from respiratory infection usually occurs before the age of fifteen years.

Trichinosis is a parasitic infestation caused by the *trichina spiralis* and contracted by eating improperly cooked infected pork. The disease, in its classical form, is divided into three stages. (1) *Ingestion*—with gastrointestinal symptoms such as nausea, vomiting, cramps, diarrhea and anorexia. These occur within a few days after eating larva. (2) *Invasion*—when the organisms are disseminated throughout the body. This stage follows the first in

from a few days to several weeks. It is accompanied by general symptoms of anorexia, chills, fever, headache and swelling about the eyes. Locally, there are muscle pain, swelling and tenderness. (3) *Encystment*—when the larva become calcified and encased in fibrous capsules. Usually this stage is asymptomatic but it may be accompanied by anemia and emaciation. Pathologically, during the stage of invasion, there are focal exudations in the muscles consisting of neutrophils, eosinophils and lesser numbers of plasma cells. While sometimes the larva may be found within these foci, they are usually not recognizable for they disintegrate rapidly. A few of the larva, however, survive and can be seen within the muscle fibers where they are surrounded by the sarcolemma. At first, they rest parallel to the long axis of the fibers, but later, they become curled,

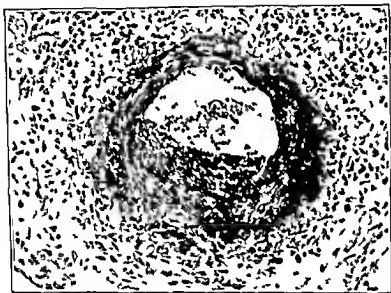


FIG. 409.—Periarteritis nodosa showing segmental fibrinoid necrosis of all the coats of the vessel. There is a diffuse arterial and perivascular infiltration with neutrophils and eosinophils. $\times 100$

calcified and surrounded by a fibrous tissue capsule. The diagnosis of trichinosis is made from the history, eosinophilia, cutaneous sensitivity tests, blood precipitin tests and muscle biopsy. The latter, in addition to being examined histologically, may also be teased out or digested by artificial gastric juice and the larvae searched for. Treatment is symptomatic. The prognosis is generally good for most infestations are not even recognized clinically. Death may occur, however, during the stage of invasion.

Periarteritis nodosa is a disease of vessels and is mentioned here only because striated muscle is frequently biopsied for diagnostic purposes. The precise cause of the disorder is not definitely known, but present indications are that it is an allergic vascularitis. It affects females three times as frequently as males and predominates in middle aged adults. Symptoms are extremely protean and depend upon the organ or organs affected. In addition, there are

remissions and exacerbations of anorexia, fever, weakness, loss of weight and leukocytosis. *Pathologically*, the process starts in the media of small and medium sized vessels whence it spreads to the intima and adventitia. The infection is most severe at points of bifurcations of the arteries. In fully developed cases, there are fibrinoid necrosis of the media and intima, fibrillation of the internal elastic lamina, encroachment upon the lumen by necrotic material and proliferated intima, and a diffuse infiltration with neutrophils, eosinophils, plasma cells, lymphocytes and erythrocytes (Fig. 409). In some cases, the walls may be so weakened that aneurysmal dilations and ruptures occur. In the healed stage, there are diffuse fibrosis of the adventitia, media and subendothelial connective tissue, fibrous occlusion or stenosis of the lumen, destruction of the internal elastic lamina, iron pigment in the adventitia, and perivascular sprinkling of plasma cells and lymphocytes. The *diagnosis* of periarteritis nodosa is difficult and can be made with certainty only by biopsy. *Treatment* is symptomatic. The *prognosis* in generalized forms of the disease has been poor, but it is probable that many infections of lesser intensity resolve.

Temporal arteritis is a granulomatous inflammation of the temporal artery of unknown etiology. It is twice as common in females as in males and occurs beyond the sixth decade of life. *Clinically*, there are pain, fever and less often malaise, weakness, sweats, photophobia and diplopia. The involved segment of the artery is prominent, nodular, exquisitely tender and if thrombosed lacks pulsations. *Histologically*, all the coats of the vessels are thickened. The intima shows a proliferation of loose edematous connective tissue, recanalization, an obliteration of the lumen and an infiltration with lymphocytes and plasma cells. The internal elastic lamina is fragmented or destroyed. The media shows an infiltration with lymphocytes and scattered plasma cells, edema and foci of necrosis. The latter are surrounded by epithelioid cells in pallisade formation and few multinucleated giant cells. The adventitia reveals a dense infiltration with lymphocytes. The *diagnosis* is made from the history and physical examination and is confirmed by biopsy. *Treatment* is symptomatic. The *prognosis* is good. Complete clinical recovery occurred in all recorded cases.

Tumors.—Although most neoplasms of connective tissue, fat, vessels, nerves and to a lesser extent of skin may involve striated muscle, there are only three that need be considered here—desmoid tumors, granular cell myoblastoma and rhabdomyosarcoma.

Desmoid tumors are benign fibromata that occur within striated muscles. They are most common in the rectus abdominis but can occur in any muscle, and predominate in women who have borne children. *Clinically*, they are discovered accidentally or they are accompanied by pain. *Grossly*, the tumor is single, oval, round or flat, is adherent to the adjoining fascias, and infiltrates between the muscle bundles so that its demarcation is poor. It is greyish white in color and firm or soft in consistency and measures as much as 15 cm. in diameter (Fig. 410). *Histologically*, it is composed of rather hyalinized fibrous tissue centrally and more cellular tissue

peripherally. The latter contains intermingled striated muscle fibers. *Treatment* is surgical excision. The *prognosis* is good.

Granular cell myoblastoma is ordinarily a benign tumor that probably arises in myoblasts. Its *synonyms* are myoblastic myoma, myoblastoma and rhabdomyome granulo-cellulaire. Over one-third of all cases have been located in the tongue, while the rest have been found in other striated muscles and in organs, such as the breast, trachea, bronchi, anus, esophagus, lacrimal sac, etc. There is no predilection for either sex and the prevalent age is beyond forty years. *Grossly*, the neoplasm is sharply circumscribed, nodular, yellowish grey or greyish white, and may measure as much as 10 cm in diameter. *Histologically*, the cells are arranged in cords, alveoli or syncytial masses and are supported by a scanty connective tissue stroma. The cells are large, sharply defined, polyhedral and have an abundant amount of coarsely granular eosinophilic cytoplasm. The nuclei are relatively small, round or



FIG. 410.—Desmoid tumor of the gastrocnemius muscle. The muscle bundles are still seen traversing the greyish white tissue.

oval, vesicular or pyknotic and usually contain a prominent nucleolus. The cells are negative for lipid and, as a rule, do not contain glycogen. The *diagnosis* of granular cell myoblastoma can be easily made by histologic study, but the uninitiated may confuse it with a xanthoma. *Treatment* is complete excision. The *prognosis* is generally good, although 10 per cent are said to be locally malignant. Distant metastasis is rare.

Rhabdomyosarcoma has the same distribution as does granular cell myoblastoma. Here, however, we are concerned only with its location in striated muscle. The muscles most frequently involved are those of the lower extremities. The tumor has no predilection for either sex and it occurs at an average age of about forty years. *Clinically*, the only manifestation is a painless tumor mass that grows rapidly or slowly, and remains deep or ulcerates through the skin. *Grossly*, the tumor is sharply circumscribed but not encapsulated. It is firm or soft, and on section is reddish grey with scattered yellow areas of degeneration and foci of hemorrhage.

Histologically, the cells are extremely variable in shape and size. Generally, however, they are large, rounded, strap-like or tear-drop shaped. The former contain two or more nuclei, while the latter usually have a single nucleus at the expanded end. The nuclei are round oval or bizarre, and vesicular or intensely hyperchromatic. The cytoplasm is usually acidophilic, granular and with careful search may disclose longitudinal myofibrils and cross striations. Less frequently, the cells are vacuolated, and without fat stains, may be mistaken for those of a liposarcoma. The stroma of dense fibrous tissue is variable in amount. Rhabdomyosarcoma is a malignant tumor. *Spread* occurs by local extension, by lymphatics and by the blood stream. The sites of metastases are the lungs, lymph nodes, skin, pleura, brain, bones, adrenals, etc. The *diagnosis* can be made only by biopsy. *Treatment* is amputation of the extremity when the lesion is favorably located and wide excision when it is not. The *prognosis* is poor. Less than 5 per cent of patients are alive five years after the lesion is discovered.

Mechanical Disturbances.—Under this heading may be considered spasmodic torticollis, hematoma of the rectus abdominis muscle, rupture of the adductor muscles of the thigh and Volkmann's ischemic contracture.

Spasmodic torticollis is a spasm of one or more muscles of the neck. The *cause* is either a psychogenic imbalance in which the nerve centers of the brain are unduly susceptible or organic changes in the basilar ganglia, encephalitis or myositis. *Clinically*, the spasm, affecting one or more groups of muscle on one or less often both sides, is either tonic or clonic. The sternocleidomastoid, trapezius and splenius are most frequently involved and the chin is rotated upward, outward and to the opposite side. Pain is a symptom in advanced cases. *Pathologically*, the muscle is shortened and greatly broadened. The fibers are hypertrophied and when the spasm is prolonged there is an accompanying and permanent fibrosis. *Surgical treatment*, used only after medical treatment has failed, consists of tenotomy, myotomy and rhizotomy.

Hematoma of the rectus abdominis muscle occurs as a result of trauma in soldiers, in athletes, in third stage of labor or coughing during pregnancy and spontaneously in muscles that are the seat of Zenker's degeneration. The latter commonly occurs in typhoid fever and influenza. The vessel most often affected is the inferior epigastric artery. Clinically, there are pain, a firm tender mass that measures to 12 cm. in diameter or more, and ecchymosis of the anterior abdominal wall. *Treatment* is symptomatic, but many are inadvertently operated upon.

Traumatic rupture of the adductor muscles of the thigh is caused by a heavy blow or by a sudden strain. The upper end of the muscle continues to function and upon contraction forms a bulky subcutaneous mass. The lesion is accompanied by pain and weakness.

tment consists of doing nothing, attempt at repair, or excision. ture of the abductors is to be differentiated from *herniation*. latter is a protrusion of the muscles through holes in the fascia are present congenitally or are formed as a result of trauma or

mersion in removing fascia for transplants. Unlike rupture, a herniated muscle bulges when relaxed and disappears when contracted.

Volkman's ischemic contracture is a contraction of a muscle due to arterial ischemia. As a result of a deprivation of blood, there is massive necrosis of muscle and degeneration of the remaining fibers. The necrosis induces a sterile inflammation which results in proliferation of the supporting connective tissue. The latter in turn becomes dense and contracts, thereby, eventuating in permanent shortening of the affected muscle.

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